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THE SEARCH FOR IMMUNOLOGICAL RELATIONSHIP BETWEEN "Q" FEVER AND OTHER RICKETTSIOSES.

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and

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It is important to define the relationship, if any, between "Q" fever and other rickettsioses. Attention has already been drawn⁽¹⁾ to the differences from "Q" fever of murine typhus and scrub typhus. This paper extends the observations to include also louse typhus and many of the large group of tick-borne rickettsioses.

Part I records the testing of a variety of sera with an emulsion of *Rickettsia burneti*, the causative organism of "Q" fever. Part II shows that Rocky Mountain spotted fever vaccine will not protect guinea-pigs against "Q" fever.

Part I: Agglutination Tests with Serum from Patients or Animals Infected with other Types of Rickettsia.

Through the kindness of workers on rickettsial diseases in various parts of the world we have received serum taken after infection of human beings or animals with most of the known pathogenic *Rickettsia*. Specimens of human serum of the following types were tested at the Walter and Eliza Hall Institute, Melbourne: endemic typhus from Queensland and South Africa, scrub typhus from Queensland, tick-bite fever of South Africa,⁽²⁾ and Rocky Mountain spotted fever. All were completely "negative" when tested with *Rickettsia burneti* emulsion at a final dilution of 1 in 10 under

standard conditions. Known "positive" and "negative" samples were included in every test.

Specimens of serum from sheep infected with heartwater from Onderstepoort and with tick-borne fever from Scotland⁽³⁾⁽⁴⁾ were also "negative". Specimens of guinea-pig serum from animals which had been infected with Rocky Mountain spotted fever, tick-bite fever of South Africa and a rickettsial infection of hares from South Africa⁽⁵⁾ were tested, again with completely negative results. Serum from a bovine in Algeria suffering from a rickettsiosis⁽⁶⁾⁽⁷⁾ was also "negative". Table I contains the details of these specimens of serum.

With reference to tick-borne fever of sheep, we have been able, through the courtesy of Dr. W. S. Gordon, of Scotland, to examine a blood slide showing the organism suspected of transmitting this disease. We agree with Dr. Gordon that this organism is entirely different from *Rickettsia burneti*, both in morphology and in the type of cell in which it is found.

In addition to the tests carried out in Melbourne, Dr. A. Pijper, of Pretoria, has kindly tested a number of specimens of human serum from the various South African rickettsial infections with "Q" rickettsial emulsion sent to him from Melbourne. The emulsion, which was sent in saline solution containing one part in 10,000 of merthiolate, appeared to retain its full agglutinability, as testing

of one of the "positive" specimens of serum sent with it resulted in full titre agglutination. Testing of the other specimen of serum indicated a moderate fall in titre. Stained films of the emulsions showed well-preserved *Rickettsiæ*. Table II gives Dr. Pijper's results with his notes on the serum used. It will be seen that his series includes three cases of louse typhus (from Port Elizabeth district) as well as endemic typhus and tick-bite fever.

In addition to the positive finding that specimens of serum from human beings or animals who have been infected with "Q" fever are agglutinated specifically with *Rickettsia burneti*, there is the equally significant negative finding that these types of serum do not agglutinate *Proteus* X strains. Rabbits inoculated with typhus *Rickettsiæ* very readily develop agglutinins to *Bacillus proteus* X 19, while guinea-pigs as a rule give little or none. It was therefore of interest to determine whether the inoculation of "Q" fever material would provoke even a small appearance of *Proteus* X 19 agglutinins in rabbits.

Two rabbits were inoculated intravenously with washed rickettsial emulsion, as used for agglutination, in two doses of two cubic centimetres at twenty-seven days' interval. Both these rabbits developed a very high agglutinating titre for *Rickettsia burneti*, 1 in 800 and 1 in 1,600. Despite this high titre for the *Rickettsia*, *Proteus* strains

TABLE I.

Details of Serum Tested with Negative Results against *Rickettsia Burneti* Emulsion.

Disease.	Species.	Distinguishing Mark.	From Whom Received.
Endemic (murine) typhus	Human.	Al.	Dr. E. H. Derrick, Brisbane.
	Human.	La.	Dr. A. Pijper, Pretoria.
Scrub typhus (K)	Human.	Bu.	Dr. R. Y. Mathew, Cairns.
	Human.	Fl.	Dr. E. A. Richards, Cairns.
	Human.	St.	
	Human.	Vi.	
	Human.	Ur.	
Rocky Mountain spotted fever	Human.	1326	Dr. G. E. Davis, Hamilton, Montana.
	Human.	1327	
	Guinea-pig.	10659	
	Guinea-pig.	10683	
South African tick-bite fever	Human.	Wa.	Dr. A. Pijper, Pretoria.
	Human.	Pr.	
	Guinea-pig.	1011	
	Guinea-pig.	1016	
	Guinea-pig.	1026	
Tick-borne fever of Scotland	Sheep.	658	Dr. W. S. Gordon, Edinburgh.
	Sheep.	659	
	Sheep.	660	
	Sheep.	661	
Heartwater	Sheep.	46053	Dr. P. J. du Toit, Onderstepoort.
	Sheep.	45972	
	Sheep.	47079	
Rickettsial infection of hares	Guinea-pig.	—	Dr. P. J. du Toit, Onderstepoort.
Bovine rickettsiosis	Bovine.	—	Dr. A. Denatien, Algiers.

TABLE II.
Comparison of *Proteus* Strains and *Rickettsia Burneti* with Human Serum (Piper).

Source of Serum.	Titre with three strains of <i>Bacillus proteus</i> .			Agglutination of "Q" Fever <i>Rickettsia</i> in Serum Dilutions.					
	Proteus X 19	Proteus X 2	Proteus X K	5	10	20	30	60	120
J. "Q" fever	—	—	—	—	—	—	++	++	—
D. "Q" fever	—	—	—	—	—	—	+++	++	±
1. Louse typhus ¹	800	160	30	—	—	—	—	—	—
2. Louse typhus ¹	320	160	60	—	—	—	—	—	—
3. Louse typhus ¹	2500	50	100	—	—	—	—	—	—
4. Rat-flea typhus	1280	480	40	—	—	—	—	—	—
5. Rat-flea typhus	240	480	30	—	—	—	—	—	—
6. Rat-flea typhus	960	960	80	—	—	—	—	—	—
7. Rat-flea typhus	240	120	40	—	—	—	—	—	—
8. Tick-bite fever	960	Not done	Not done	—	—	—	—	—	—
9. Tick-bite fever	—20	—20	40	—	—	—	—	—	—
10. Tick-bite fever	80	40	20	—	—	—	—	—	—
11. Tick-bite fever	30	—20	—20	—	—	—	—	—	—
12. Tick-bite fever	30	20	10	—	—	—	—	—	—
13. Tick-bite fever	120	60	60	—	—	—	—	—	—

¹ Specimens 1, 2, 3 (louse typhus) were obtained through the kindness of Dr. Gray, of the Port Elizabeth laboratory.

OX19, OXK, X2 and XL showed no significant agglutination. One specimen of serum agglutinated OXK to a dilution of 1 in 20. The others showed only traces of agglutination at that dilution. Control tests of the OXK emulsion with known scrub typhus serum showed full agglutination to a serum dilution of 1 in 1,000.

From this series of negative results we may justifiably conclude that "Q" fever has no antigenic relationship to any of the previously known human infections due to *Rickettsia*.

There are two important human rickettsioses from which types of serum have not been examined for "Q" agglutination—*fièvre boutonneuse* and Indian tick typhus. These are known to differ serologically from "Q" fever in giving agglutination with *Proteus* OX2 and OX19. The omission of these types of serum from the present work does not therefore invalidate the conclusion given above.

The first patient with tick-bite fever (Table II) gave an unusually high titre for this disease. Serum from patients with the other tick-bite fevers was taken during fever; such serum always gives a poor titre. It will be noted that both louse typhus and rat-flea typhus in South Africa agglutinate *Proteus* X2 quite well and often *Proteus* XK also. No agglutination ever occurred with the "Q" fever emulsion.

Part II: Failure of Rocky Mountain Spotted Fever Vaccine to Protect Guinea-Pigs against "Q" Fever.

The possibility of a relationship between "Q" fever and Rocky Mountain spotted fever has been investigated here in two ways: (i) testing of spotted fever immune serum for "Q" agglutination (the results of these tests are recorded in the first part of this paper); (ii) vaccination of guinea-pigs with spotted fever vaccine and subsequent inoculation with "Q" virus. These results are reported below.

A vaccine for the prevention of Rocky Mountain spotted fever is prepared in the Rocky Mountain

Laboratory at Hamilton, Montana, from the ground bodies of infected ticks.⁽⁸⁾ One mil of the vaccine will fully protect four out of six guinea-pigs against a subsequent injection of one mil of guinea-pig spotted fever passage virus. The vaccine has been used with considerable success in the prevention of human infection.

Guinea-pigs inoculated with the vaccine are protected against Sao Paulo fever, which is important evidence of its essential identity with Rocky Mountain spotted fever.⁽⁹⁾

To enable us to make similar tests with "Q" fever, Dr. G. E. Davis, acting director of the Rocky Mountain Laboratory (in the temporary absence of the director, Dr. R. R. Parker) kindly sent to Brisbane a supply of spotted fever vaccine.

Five guinea-pigs (J286 to J290) were each given a subcutaneous injection of one mil of the vaccine. Eleven days later they were inoculated intraperitoneally with "Q" virus, in the form of one mil of liver-spleen emulsion from an infected guinea-pig. Each reacted with "Q" fever in a manner identical with the two unvaccinated controls (Figure I).

Another series of five guinea-pigs (J274 to J278) were each given two doses of the vaccine at an interval of eleven days, and were then inoculated with one mil of "Q" virus after another eleven days. These also were not protected. The latter experiment was begun eleven days before the one previously described, so that all the guinea-pigs could be inoculated with the same "Q"-infective emulsion.

The "Q"-immune controls each received two mls of the emulsion. They remained afebrile for fourteen days.

The guinea-pigs used in the experiments all weighed between 250 and 290 grammes, except two of the controls—J284 (312 grammes) and J265 (325 grammes).

There was some delay in the making of our tests with the vaccine, which was manufactured in May,

1937, and used in May, 1938. As we were not aware of its keeping qualities, the balance of the supply was returned to Dr. Parker, who kindly retested it. He wrote as follows:

The vaccine which you returned has been tested and its potency is still good. Five guinea-pigs were injected with one cubic centimetre each and ten days later tested against spotted fever virus. Four were completely immune, while the fifth ran a low, irregular temperature, which may or may not have been due to Rocky Mountain spotted fever. Your tests, therefore, can be taken at face value.

Rocky Mountain spotted fever vaccine will not, therefore, protect guinea-pigs against "Q" fever.

"Q" virus, in the form of infected mouse spleens, and samples of "Q" immune serum were sent to Dr. R. E. Dyer, chief of the Division of Infectious Diseases, United States Public Health Service. Dr. Dyer's results support our own. He wrote as follows:

I succeeded in carrying out one or two cross immunity tests between the "Q" fever strain and a strain of endemic typhus and a strain of Rocky Mountain spotted fever. Apparently "Q" fever gives no immunity to either Rocky Mountain spotted fever or endemic typhus, nor do the two latter diseases immunize against "Q" fever.

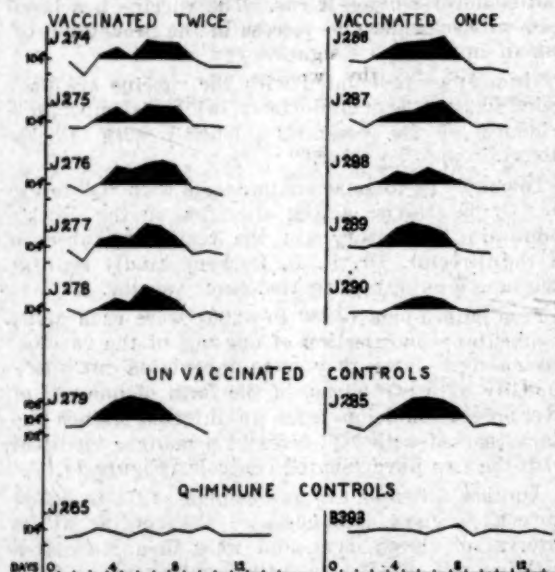


FIGURE 1.

Temperature charts of guinea-pigs vaccinated with Rocky Mountain spotted fever vaccine and then (on "Day 0") inoculated with "Q" fever. The charts show that the vaccine did not protect against "Q" fever.

The Relation of "Q" Fever to an Infection Isolated from Ticks in Montana.

Officers of the United States Public Health Service have isolated a filter-passing infectious agent from Rocky Mountain wood ticks (*Dermacentor andersoni*) captured in Montana.⁽¹⁰⁾ The agent appears to be a *Rickettsia*. It is capable of causing human infection. The infection, both in man and in laboratory animals, has many points of resem-

blance to "Q" fever. There are also definite points of difference.

Dr. Dyer found that five guinea-pigs which had recovered from "Q" fever were subsequently immune to the Montana virus; he also found that the serum of two patients convalescent from "Q" fever gave definite protection to guinea-pigs against the Montana virus. These findings indicate a relation between the two diseases. Further work to elucidate the point is proceeding both in America and in Australia.

Summary.

1. Serum from patients or animals suffering from most of the known rickettsioses has been tested for agglutination with an emulsion of *Rickettsia burneti*, with negative results.
2. Guinea-pigs injected with a vaccine which will protect against Rocky Mountain spotted fever are not thereby protected against "Q" fever.
3. Our results show no evidence of immunological relationship between "Q" fever and the rickettsioses tested; but attention is drawn to work by Dyer indicating a relationship between "Q" fever and an infection obtained from ticks in Montana.

Acknowledgements.

Our thanks are due to the workers in many parts of the world, whose names are mentioned in the body of the article, for their kind cooperation in sending us serum and vaccine, and in permitting us to refer to work performed with "Q" fever material in their own laboratories.

We are indebted to Sir Raphael Cilento, Director-General of Health and Medical Services, Queensland, for permission to publish that part of this work which was performed in Brisbane, and to Mr. H. E. Brown, bacteriologist, for his assistance.

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PREECLAMPTIC TOXÆMIA.¹

By IRVING BUZZARD,
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I HAVE selected for my subject "Preeclamptic Toxæmia". This term is used because the older term, "albuminuria of pregnancy" is misleading, since it refers to a sign (albumin in the urine) which is frequently seen later than the other signs (œdema and elevated blood pressure) and not infrequently does not occur at all. F. J. Browne defines preeclamptic toxæmia as "a condition occurring in pregnant women characterized chiefly by a rise in blood pressure, œdema and albumin in the urine and often ending in convulsions". Further, by using the term "albuminuria of pregnancy" one might be expected to include cases of an underlying nephritis, or essential hypertension coexisting with pregnancy; and time would not permit of my discussing these.

Ætiology.

Eclampsia may be considered the end stage of the preeclamptic toxæmia, and so the ætiology of both can be considered together. The many theories propounded make most entertaining reading. None are entirely satisfactory, and as they are speculative, I shall briefly mention a few of the more popular.

1. The "intestinal toxin" theory, commonly known as the "Dublin" theory, was promulgated by Tweedie in 1913. Normally antibodies in the blood stream are sufficient to neutralize toxins of food and toxins of pregnancy; but if there is an excess of food poisons or amino-acids, these antibodies may be insufficient and toxæmia may result.

2. The "placental" theory was put forward by Young in 1914. Infarction of the placenta takes place, and from the dead placental area toxins are liberated into the blood stream. This infarction admittedly occurs; but whether it is a cause or a result of toxæmia is still a debatable point.

3. The "water" theory was propounded by Zangemeister in 1915. He held that eclampsia could be produced by retention in the tissues of fluid, the result of increased permeability of the capillary walls. General œdema was brought about as well as œdema of the brain, with an accompanying anæmia; the brain was rendered more irritable to stimuli, hence the convulsions. However, toxæmia and even eclampsia occur without œdema; moreover, the cause of the increased permeability of the capillary walls is not explained.

4. The "increased abdominal pressure" theory of Paramore is that the enlarged uterus leads to circulatory upset in liver and kidneys. This theory is supported by the fact that the incidence of toxæmia is increased with twin pregnancy; but the same would be expected to occur in the presence of a large abdominal tumour.

5. The "endocrine" theory, suggested by Hoffman and Kennedy, is that the pituitary gland secretes substances that raise the blood pressure and cause œdema. Naturally, these are in excess in eclampsia. Other authorities hold that there are a deficiency of *corpus luteum* and an excess of œstrin. However, these findings have not been confirmed.

6. The "dietetic deficiency" theory, as propounded by Theobald, has for its basis the supposition that a diet sufficient for an ordinary woman is insufficient for a woman and a fetus. He believes that whilst the responsibility rests with a deficiency in vitamins and minerals, the most important single factor is a disturbance in calcium metabolism. Interesting is the fact that in Germany during the War, which implied years of under-feeding, the incidence of eclampsia fell from 2.0 per 1,000 to 0.6 per 1,000. Here there is a deficiency in meat, calcium and vitamins A, B and D. Theobald states that the more animal protein that is ingested, the more calcium and vitamins A and D are required. Thus, in Germany the scarcity of animal protein more than compensated for the deficiency in calcium and vitamins. In India it is interesting to note that the incidence of toxæmia is 3% for the Hindus and 1.66% for Mohammedans; yet the latter are meat eaters and the former eat no meat at all. Theobald's figures are significantly stimulating. He selected 100 healthy women twenty-four weeks pregnant. To the first group he gave calcium with vitamins; the second group served as controls. The incidence of toxæmia was two and a half times greater in the second group. Medenhall and Drake found that only 1% of approximately 200 patients developed toxæmia when calcium was given, whilst in the control group the incidence was 13%. As you see, the fundamental cause of toxæmia is still obscure; but, to quote Browne, "the immediate cause of eclamptic convulsions is the hypertension with or without œdema of the brain and its membranes". It therefore naturally follows that a sudden rise in blood pressure is more likely to cause convulsions than a slow, steady increase. Also, if cerebral œdema is present, not such a large rise in blood pressure is required for the production of convulsions.

Pathology.

From the maze of ætiological theories I shall briefly gloss over the pathology. Schmorl has shown that the main changes in the organs are in the nature of thromboses of capillaries and small veins and occasionally of arterioles, with hæmorrhages and necrosis in the areas immediately surrounding them. The organs chiefly affected are the liver, kidneys, central nervous system, heart, lungs and pancreas.

Clinical Course.

Preeclamptic toxæmia occurs in about 3% of cases. It is rarely seen before the twenty-eighth week and usually occurs from the thirty-second week onwards. Incidence is much greater in *primipara*.

¹ Read at a meeting of the Victorian Branch of the British Medical Association on May 6, 1939, at Warrnambool.

Signs.

Generally the first sign is a rise of blood pressure above the normal figures (systolic, 130, diastolic, 70, millimetres of mercury). The next sign is oedema, mainly affecting the feet, ankles and fingers. Even weeks may elapse before albumin appears in the urine. The amount of albumin is only a trace at first—in fact, it does not show in every specimen; but it usually proceeds rapidly to a heavy deposit.

If the patient remains untreated, the following symptoms may be expected to appear: (i) visual disturbances, such as diminution of vision, black specks before the eyes *et cetera*; (ii) headache, very early and very constant; (iii) vomiting and epigastric pain; (iv) oliguria, with increased oedema and blood pressure. These are indications of increased intracranial pressure, and the onset of convulsions is not far off. Again I stress the point that eclamptic convulsions can occur without the warning signs of albuminuria and oedema, though in this event the increase in blood pressure is more pronounced.

Examination of the *fundus oculi* may give us some useful information, revealing some oedema of the retina and in severe cases "cotton wool" patches of exudate and hæmorrhagic areas in the retina. Examination at frequent intervals is helpful. Further, the appearance of "cotton wool" patches or detachment of the retina is an indication for termination of the pregnancy. The state of the retinal vessels is of help in differential diagnosis. Arteriosclerosis indicates a preexisting renal or arterial disease, whilst its absence indicates either a toxæmia or a chronic nephritis, without systemic changes.

An increase of over five pounds in the patient's weight in any one month should be taken as a warning of possible toxæmia. It should not, however, be inferred that all patients who gain more than five pounds in weight are toxæmic; neither does the converse hold true.

Investigations of the blood chemistry reveal little or no change, and the results of renal function tests are not appreciably altered. They are mainly a help in the differentiation between chronic nephritis and hypertension.

*Treatment.**Prophylactic Treatment.*

Naturally, in discussing the treatment one first thinks of prophylaxis. The first essential is the early recognition of the warning signs. In my own practice I ask all patients to see me every fourteen days after the twenty-eighth week, and every seven days after the 34th week. The examination of the urine alone is not sufficient; the blood pressure must be estimated and signs of oedema looked for. I weigh most of my patients; but as yet I have not encountered one whose weight increased more than five pounds in a month. With further reference to prophylactic treatment, I must confess to a liking for the "dietetic deficiency" theory of Theobald. My regret is that the calcium requirements and the calcium deficiency cannot be measured scientifically,

for it would be possible then to know how much calcium should be given. I now give 1.0 to 1.2 grammes (15 to 20 grains) of calcium gluconate per day. The diet I recommend is the usual balanced diet, with plenty of vitamins, and sea fish twice a week as a source of phosphorus.

General Treatment.

I again emphasize the statement that an early rise of blood pressure above the normal figures is usually the first sign of toxæmia and precedes the albuminuria by weeks. The blood pressure is of necessity estimated with the patient in the recumbent position. If her systolic blood pressure is between 135 and 140 millimetres of mercury I allow her to go home, to remain in bed for forty-eight hours; her daily diet is to be five pints of barley water and glucose, an abundance of fruit and 3.0 grammes (45 grains) of calcium gluconate. If her condition improves I allow her to rest at home and promote her to Stage II of the following diet used in Guy's Hospital maternity department:

Fluids and fruit (as above).

Breakfast: Toast, two ounces; butter, half an ounce; marmalade *et cetera*, one ounce; tea.

Lunch: Cocoa or coffee.

Dinner: Sandwiches ("Marmite", lettuce *et cetera*), two ounces; pudding, four ounces; jam, one ounce.

Tea: Bread, two ounces; butter, half an ounce; jam, half an ounce; tea.

Supper: Biscuits, one ounce; cocoa.

This diet is illustrative and not rigidly adhered to.

If the patient's condition further improves, as judged by her blood pressure, she is allowed to move about, and I promote her to the Stage III diet. This is as follows:

Breakfast: Toast, two ounces; butter, half an ounce; marmalade *et cetera*, one ounce; tea.

Lunch: Cocoa or coffee.

Dinner: Sandwiches, four ounces; vegetables *ad libitum*; pudding, four ounces; jam, one ounce.

Tea: Bread, two ounces; sandwiches, one ounce; tea.

Supper: Biscuits or sandwiches, one ounce; coffee or cocoa.

I make the patient adhere to this diet until she is delivered, although I see her every second or third day. Many writers contend that, once established, toxæmia will not disappear entirely until delivery. My experience differs from this, and my opinion is that very early toxæmia can in some instances be cleared up. If the patient's condition does not improve, or if her systolic blood pressure is over 140 millimetres of mercury, she is admitted to hospital, where her blood pressure and the results of her urine tests are recorded daily. She is now under constant observation, and any of the aforementioned danger signs are easily recognized and acted upon. In these cases I give an initial enema and see that there is a good bowel action daily. If oedema is present the diet is kept free from salt, and if albuminuria is present the urine is kept alkaline to litmus by means of large doses of potassium citrate *et cetera*. Apart from this, the dietetic treatment is as I have outlined.

I come now to those patients whose systolic blood pressure is between 150 and 170 millimetres of mercury, and whose urine frequently contains more than a trace of albumin and who have some oedema. These patients call for rigid and strict supervision in hospital. They are given an enema, followed by a bowel wash-out, and then the treatment outlined above. If there is no improvement in a few days, pregnancy must be terminated. Even if an improvement does occur, the view is generally accepted that temporizing measures should not be continued after fourteen days, otherwise delay will lead to permanent damage of the kidneys or to hypertension. Occasionally, in the case of an elderly *primipara*, one may be tempted to try to tide the patient over to the thirty-fourth week; the risks attendant on this procedure must be carefully explained to the husband. After delivery, the patient is given Stage III diet for about ten days, and then Stage IV diet, which means the addition of fish, eggs and half a pint of milk daily.

Termination of Pregnancy.

The best means of avoiding eclampsia and the risk of chronic nephritis, hypertension, a tendency to recurrence of toxæmia in subsequent pregnancies and death of the foetus *in utero* is to terminate the pregnancy. Gibbard holds that as a general rule the termination of pregnancy should be advised in the following circumstances: (i) in the presence of a systolic blood pressure of 160 millimetres of mercury or more, in which there is no response to treatment within a few days; (ii) in all cases, however mild, in which albuminuria has persisted for more than two weeks; (iii) in all cases in which there is an increase in severity of the signs; (iv) in all cases of recurrent toxæmia, in which a macerated foetus occurred in a previous pregnancy, as soon as the foetus is large enough to have a reasonable chance of being viable. The question is not whether the termination is justifiable, but rather whether there is justification for not terminating the pregnancy.

The method of termination is usually rupture of the membranes, though in cases of prematurity I prefer tubal induction in conjunction with medicinal stimulation. I do not like the idea of the soft premature head having to dilate the cervix. Some authorities advocate Cæsarean section in those cases in which eclampsia seems imminent.

Reports of Cases.

In my last ten years of practice in Warrnambool, I have attended privately 1,197 patients, and have had one case of eclampsia; I think this should have been avoided.

CASE I.—Mrs. B. expected her third confinement on September 3, 1930. From her previous obstetrical history it was learned that eclampsia had occurred in her first pregnancy; everything was perfectly normal in her second. I examined her urine weekly from the thirty-second week. On September 4, 1930, her urine was perfectly clear, but a minor degree of oedema was present. On September 8, 1930, I was called to the patient, who was having eclamptic convulsions. Her systolic blood pressure was 190 millimetres of mercury and her urine was nearly solid with

albumin. She recovered well and the baby lived. The results of her renal functional tests have been normal, and she recently had a normal pregnancy and confinement for which I attended her.

The point I wish to emphasize is this: I am now sure that if I had been careful in estimating the blood pressure regularly, early toxæmia would have been suspected, and the mother and baby would not have been subjected to the risk of eclampsia.

CASE II.—Mrs. M., aged twenty-eight years, expected to be confined on December 7, 1933. Her first pregnancy had been perfectly normal twenty months previously. On October 3, 1933 (thirty-first week of pregnancy), in the course of an antenatal examination, I found that her systolic blood pressure was 138 millimetres of mercury, and that the urine contained 1% of albumin. A little oedema was present. I admitted her to hospital, and for the next four weeks (the month of October) her systolic blood pressure varied between 124 and 135 millimetres of mercury and the percentage of albumin in her urine from 0.5 to 1.0. On November 5, 1933 (thirty-fifth week), her systolic blood pressure was 140 millimetres of mercury and the percentage of albumin was 2.0. Medicinal stimulation was tried unsuccessfully. For the month of November the percentage of albumin in her urine was never below 1.25, and even rose to 3.0, whilst her systolic blood pressure varied between 128 and 150 millimetres of mercury. Medicinal stimulation was tried four times without success. Rupture of the membranes was finally carried out in conjunction with stimulating treatment on December 4 and a living baby was delivered. During this period results of the patient's kidney function tests never departed from the normal.

This patient now has a chronic nephritis. She may have had an underlying nephritis beforehand, and pregnancy, that certain test of kidney function, may have caused it to light up. I, however, regard the case as one of toxæmia. Whatever it was, I was wrong in allowing the pregnancy to progress for eight weeks; I relied on the normal results of the kidney function tests. I have advised the patient against subsequent pregnancies, and *post hoc* or *propter hoc* her husband left her soon after the birth of the child. This is a case in which in the interest of the mother pregnancy should have been terminated some weeks earlier.

CASE III.—Mrs. F.B. expected to be confined on October 30, 1935. She was a *primipara*, aged twenty-five years. On September 3 her blood pressure was normal and no albuminuria or oedema was present. On September 17 her systolic blood pressure was 135 and her diastolic blood pressure 80 millimetres of mercury; but no albuminuria or oedema was noted. On September 24 her systolic blood pressure was 140 and her diastolic blood pressure 80 millimetres of mercury; slight oedema was present, but no albuminuria. She was allowed to go home and was instructed to have a protein-free diet. On September 30 her systolic blood pressure was 140 and her diastolic blood pressure 90 millimetres of mercury; the oedema was more pronounced and her urine was loaded with albumin. She was immediately sent to hospital and given the eliminative treatment so popular at that time. The results of her kidney function tests were normal. Her condition improved, but not satisfactorily. On October 9, that is, at the thirty-seventh week, I terminated pregnancy by tubal induction combined with medicinal stimulation, and she was delivered of a healthy baby weighing six pounds. She has been in good health since; she expects to be confined in July, and is perfectly well up to the present time.

This case illustrates the fact that a rise in blood pressure can occur before albumin appears in the urine.

CASE IV.—Mrs. R., aged twenty-eight years, was pregnant for the third time and expected to be confined on February 18, 1939. There was nothing of interest in her previous history. On January 14 (thirty-fifth week) a little oedema and a trace of albumin in the urine were present, and her systolic blood pressure was 145 and her diastolic blood pressure 90 millimetres of mercury. She was admitted to hospital and the usual treatment was given. She was discharged on January 21; on that date her systolic blood pressure was 126 and her diastolic blood pressure 80 millimetres of mercury, and no albuminuria or oedema was present. I saw her two or three times a week, till she was delivered on February 20, 1939. Since then her blood pressure has been normal and her urine clear.

I regard this case as of one of the milder toxæmias, which cleared up with treatment.

CASE V.—Mrs. S., aged twenty-three years, a *primipara*, expected to be confined on April 27, 1939. On March 7 (thirty-third week) her systolic blood pressure was 140 and her diastolic blood pressure 70 millimetres of mercury. No albuminuria or oedema was present. She responded at once to treatment by rest and starvation and remained normal till March 29. Her systolic blood pressure then was 136 and her diastolic blood pressure 80 millimetres of mercury; the urine contained a very slight trace of albumin and no oedema was present. She was given the usual treatment at home. On March 31 her blood pressure was the same as before, but there was a little more albumin in the urine and the ankles were slightly oedematous. She was admitted to hospital for seven days and her condition returned to normal. Since then she has been perfectly well; on May 3 her systolic blood pressure was 124 and her diastolic blood pressure 76 millimetres of mercury, and no albuminuria or oedema was present. She was delivered on May 4, and both mother and baby are perfectly well.

In my opinion this is another case of mild toxæmia in which treatment was successful.

Conclusion.

Whilst the ætiology of preeclamptic toxæmia is still obscure, from my experience I can only state that it is impossible to over-estimate the importance of early and frequent estimation of the blood pressure.

A SUMMARY OF MODERN VIEWS ON THE FEMALE SEX HORMONES AND THEIR SCOPE IN THERAPY.¹

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I HAVE been asked to speak on the subject of female sex hormones, firstly because of its absorbing interest, secondly to point out the underlying principles of the physiology of the female sex hormones, and lastly to indicate the most successful phases of sex hormone therapy. It is hoped that a fuller understanding of the physiology will be gained thereby, and, more importantly, that some points of practical use in therapy will be brought out.

¹ Read at a meeting of the Eastern Suburbs Medical Association on May 5, 1939.

The Endocrine Set-Up.

The endocrine set-up and the interaction of the various sex hormones are shown diagrammatically in Diagram I. In this paper only the pituitary-ovary axis and the ovary-uterus axis will be considered.

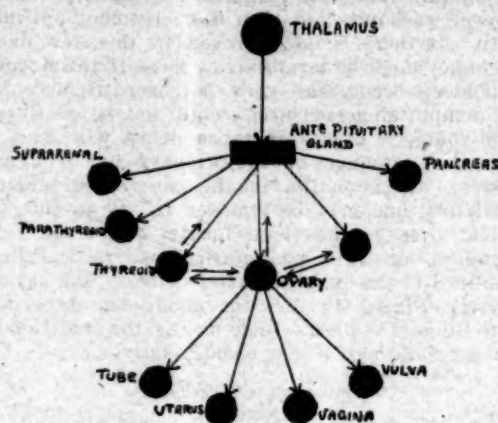


DIAGRAM I.

It is known that the anterior pituitary gland secretes a hormone called the gonadotropic hormone. This hormone stimulates the ovary. It is said to be differentiated into two different hormones, one called prolans A, which directly stimulates the growth of the Graafian follicle, and the other called prolans B, which stimulates the formation and the growth of the corpus luteum.

During the early months of pregnancy large amounts of this gonadotropic hormone (both A and B) are found in the blood. Also large quantities of a gonadotropic-like hormone are found in the urine of pregnant women during the early months of pregnancy. It is on this latter fact that the now famous Aschheim-Zondek test for pregnancy is based.

It is thought that, during the early months of pregnancy, the placenta takes on the production of these large quantities of gonadotropic hormones. Thus we see that the anterior pituitary sex hormone, commonly called the gonadotropic hormone, has two functions, or, what is more probable, actually consists of two hormones, one the follicle-stimulating hormone (prolans A) and the other the luteal-stimulating hormone (prolans B).

The ovarian tissue, under the influence of these hormones, produces one mature Graafian follicle, ovulation, and then a corpus luteum during each menstrual cycle. The action of prolans A predominates in the first half of the cycle and that of prolans B in the second half of the cycle. The growing and mature follicle produces a sex hormone, the ovarian follicular hormone, called oestrin or folliculin. This has a direct action on the genital tract, stimulating growth and contractions of the tube and uterus, and growth in the mucous membranes of the vagina and the vulva. These effects can be studied by lipiodol injections, by measurements

of the length of the uterus, by vaginal smears to determine the number and size of the vaginal squames and by the increase in the size of the vulva respectively.

Œstrin also has a stimulating effect on the pelvic sympathetic nervous system. Œstrin (folliculin) has a back action on the anterior pituitary gland; that is, it neutralizes the action of the anterior pituitary hormone and thus in large doses it has a depressing action on the anterior pituitary gland. Large doses of œstrin have cured the severe anterior pituitary headache encountered occasionally in pregnancy. Œstrin will sensitize a uterus, particularly when a "missed labour" occurs, and more so when there is a missed abortion and the foetus is dead. Œstrin has a direct action on breast tissue to stimulate the growth of the periductal tissue and growth of ducts themselves.

After ovulation, which takes place about the thirteenth to the fifteenth day of the menstrual cycle, the *corpus luteum* is formed. This produces a sex hormone called the luteal hormone, lutein or progesterin. The known effect of this is to inhibit the action of œstrin, to inhibit uterine contractions, to depress the pelvic sympathetic nervous system, causing a dilatation of blood vessels. This effect gives rise to the bluish colour of the genitals at the menses and in early pregnancy. Progesterin also stimulates the growth of the milk glands in the breast. It is responsible for the induction of the secretory phase of the endometrium. It desensitizes the uterus to the influence of the posterior lobe of the pituitary gland.

The Menstrual Cycle and the Hormones.

From the scheme of the physiology of the menstrual cycle shown in Diagram II it can be seen that in the first half of the cycle œstrin stimulates the growth of the glands and the stroma cells, that is, the stage of proliferation; and in the second half progesterin stimulates secretion of the glands and also growth of the stroma cells, producing at about the twenty-seventh or twenty-eighth day a decidual reaction. This takes place in the outer or compact layer of the endometrium. Should an impregnated ovum arrive, it is embedded in these cells, which, under the influence of the *corpus luteum* of pregnancy, form the decidua.

Also the second half of the menstrual cycle is sometimes known as the secretory stage. The endometrial glands grow and their lining columnar cells swell with secretion and finally pass this secretion into the lumen of the glands, which swell up and become elongated and like cork screws.

Thus it is seen how the balanced action of the two ovarian hormones (œstrin and progesterin) produces the changes in the endometrium throughout the menstrual cycle.

Old text-books on gynaecology sometimes described the bleeding of menstruation as comparable to the red flag at the auctioneer's door, indicating that something more important was going on inside. At the present time it is realized that very important

things are happening inside and the full significance of these things is being gradually understood.

It is to be remembered that the two ovarian hormones controlling the menstrual cycle are under the direct influence of the gonadotropic hormone from the anterior pituitary gland.

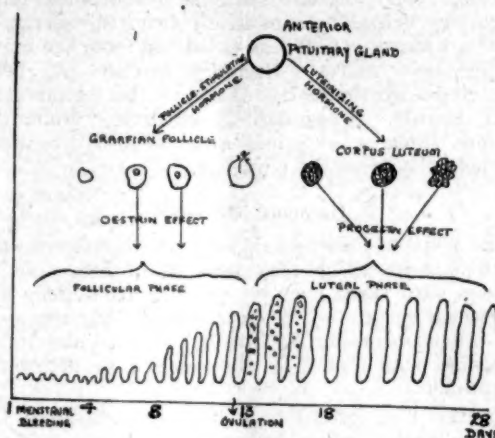


DIAGRAM II.

The concentration of the female sex hormones in the blood during the various phases of a woman's life are shown in Diagram III, a, b and c.

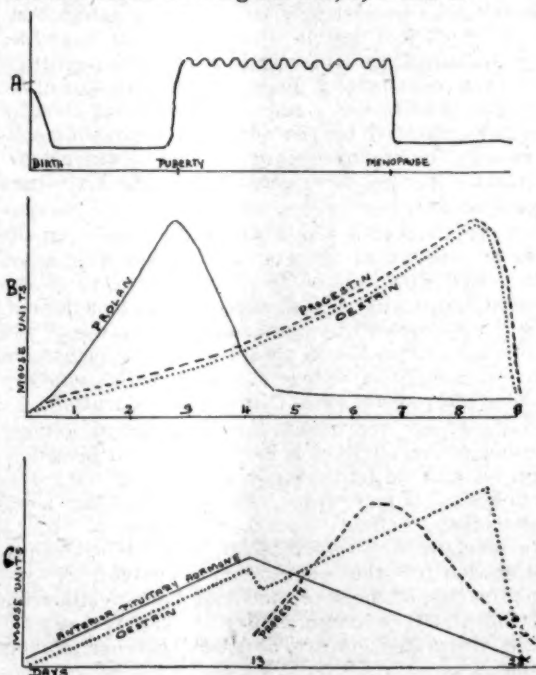


DIAGRAM III.

Showing concentration of sex hormones in the blood of the female: A, throughout life; B, in pregnancy; C, during the menstrual cycle.

The gonadotropic hormone is produced by the anterior pituitary gland, and during pregnancy is

produced by the placenta. Œstrin is produced by the Graafian follicle, and during pregnancy by the chorion. Progesterin is produced by the *corpus luteum* and during pregnancy by the *corpus luteum* of pregnancy.

These hormones are prepared from the following sources. Gonadotropic hormone is obtained from pregnancy urine and also lately from the serum of pregnant mares. Œstrin is extracted from the urine of pregnant mares. Recently Œstrin has been extracted synthetically under the name of "Stilbœstrol". Progesterin is extracted from the *corpora lutea* of whales, and is now produced synthetically from the soya bean.

Hormone Therapy.

The scope of hormone therapy, in other words the conditions in which they may be of use, may be divided into three groups: (a) deviation from the menstrual cycle; (b) the hæmorrhages of pregnancy and other pregnancy conditions; (c) the multiform disorders which may be summarized as deficiency symptoms.

To the first group may be said to belong the various types of amenorrhœa.

In primary amenorrhœa, which occurs usually with genital hypoplasia, and which may be defined as a complete lack of spontaneous bleeding in women from the age of eighteen and beyond, hormone therapy achieves lasting success only in exceptional cases. Sufficient Œstrin (folliculin), for example, may produce a certain development of the genitals and even occasionally bring on bleedings, but it very rarely brings on a normal cycle. These results are not improved by the addition of gonadotropic hormones or by pregnancy blood transfusions. Hormone therapy for primary amenorrhœa is not recommended.

Of greater value, on the other hand, is the hormone treatment of secondary amenorrhœa, when the actual duration of the amenorrhœa is of the utmost importance if real success is to be achieved. Many well-known observers have, by the use of sex hormones, been able to obtain a regular menstrual cycle in a high percentage of women with secondary amenorrhœa of not more than a year's duration.

Before any treatment for irregular menstrual periods or amenorrhœa is begun, a careful investigation of the patient should be carried out; this includes a biopsy from the endometrium, basal metabolism estimation, the application of a Wassermann test to the blood, a full blood count, estimation of the blood sugar content, X ray examination of the skull and long bones, estimation of the blood creatinin content. The reasons for these investigations are outside the scope of this paper.

The following case illustrates the value of this investigation.

CASE I.—F.G., aged thirty-five years, who had had no children, complained for two years of hot flushes, depression and "nervy turns" and hypomenorrhœa. Her basal metabolic rate was found to be -24%. Treatment by

thyroid extract, 0.3 gramme (four grains) a day, cured her symptoms and brought the menses back to normal. Two years later she was still well and on thyroid extract.

The method employed by Professor Kaufmann, of Berlin, is as follows. For mild cases or just irregular periods 10,000 units of Œstrin in tablets are given orally every day for the first fifteen days of the cycle. This is repeated for three or four months. For sterility and severe secondary amenorrhœa he first of all gives biweekly injections of Œstrin, 50,000 international benzoate units, over the follicular stage, that is, the first fifteen days for the first month. He then gives biweekly injections for the first fifteen days of the second month, biweekly injections for the first fifteen days of the third month, and in the fourth month biweekly injections for the first fifteen days, followed by *corpus luteum* hormone for the second fourteen days, with 1,300 cubic centimetres of pregnancy blood transfusion.

CASE II.—E.S., aged twenty-nine years, complained of amenorrhœa for three months, and prior to that of amenorrhœa for four months. This irregularity of period followed a miscarriage. She was given four tablets (of 2,000 units each) of Œstrin a day for the first fifteen days of the cycle for three consecutive months. Following this the patient has had four regular periods at twenty-eight to thirty-one days, lasting three to five days and rather scanty. Her general health improved.

CASE III.—E.B., aged twenty-seven years, had had one child five years previously. She had amenorrhœa for four months. She had always had irregular and scanty periods and headaches. She had a course of Œstrin, similar to that outlined by Professor Kaufmann, for two months. Then she was given a course of serum gonadotropic hormone for three months. This last course of injections made her feel well and brought on menstrual-like bleeding for the past three months.

Much less successful are the results in secondary amenorrhœa of longer duration.

Recently I had successful results with treatment of weak menstruation (hypomenorrhœa). Ovarian sex hormones were used. Four injections of Œstrin in the first fifteen days and four injections of progesterin in the second fifteen days was the method employed.

CASE IV.—B.R., aged eighteen years, complained of hypomenorrhœa (weak menstruation) for twelve months. She was given Œstrin in the first part of the menstrual cycle and progesterin in the second half of the menstrual cycle for two months. This brought on two normal menstrual bleedings, and the patient felt very much improved.

Recently reports have been received from all sides of the success of Œstrin (folliculin) therapy in dysmenorrhœa, especially when this occurs together with hypoplastic manifestations in the gonads. Small doses of follicular hormone in the proliferative phase of the cycle often produce a striking improvement.

Sex hormones can also be used in the treatment of sterility.

For the cure of the short menstrual cycle 50,000 international benzoate units of Œstrin are given on the last day of the period. This extends the next cycle to twenty-eight or thirty days by inhibit-

ing the action of the gonadotropic hormone for a few days.

Œstrin is occasionally useful when a period is to be delayed two or three days (in the case of an actress or a swimmer); a massive dose is given just before the period.

The second great field for hormone therapy in gynaecology is represented by the hæmorrhages of pregnancy. Here it is the luteal hormone, the safeguarding action of which on the maintenance of pregnancy is so successfully exploited, especially against habitual abortion and premature birth.

The dosage recommended varies considerably. As a general principle in mild cases only small doses are required. For example, in the treatment of so-called delayed abortion, one weekly injection of one international unit of progestin to the seventh month is all that is necessary. In the treatment of threatened abortion, on the other hand, an injection of ten international units daily may be given.

Besides its capacity to maintain pregnancy, the extensive physiological function of progestin gives it a therapeutic value in that it restores to the proliferated endometrium the power of secretion in the normal cycle. But defective luteal action occurs, as is well known, when the follicles in the ovaries persist. The consequent excessive supply of œstrin (folliculin) leads to endometrial hyperproliferation and finally to functional bleeding due to a cystic glandular hyperplasia (*metropathia hæmorrhagica*). In isolated cases this condition can be cured by treatment with progestin.

Other uses of the sex hormones in pregnancy are: firstly, the use of œstrin in the sensitization of the uterus for the induction of labour or premature labour. This treatment is particularly effective when the fœtus has died. Secondly, œstrin may be used as an adjunct in the treatment of uterine inertia. It should be used in the treatment of those patients in whom uterine action is not improved by sedatives and antispasmodics. It not only enhances the power of the uterine contractions, but also serves to regulate and coordinate them, and this latter effect is of the utmost importance. It is especially useful in the prophylactic treatment of inertia.

The main field for gynaecological hormone therapy consists of the so-called deficiencies with their many-sided symptoms (headaches, flushes, depression *et cetera*). In this connexion substitution of the defective or totally missing follicular hormone is the surest method by which the deficiency symptoms may be influenced and is the ideal treatment.

On account of its elective action, œstrin (folliculin) can often be enlisted as an aid in the diagnosis of even those special types of deficiency symptoms which have no immediately recognizable relation to ovarian dysfunction. Thus the use of follicular hormone (œstrin) is undoubtedly the most effective treatment for *pruritus vulvæ* known today. But other lesions of the skin such as eczema, *ulcera cruris et cetera*, can also occasionally be cured by the administration of œstrin, in so far as they are conditioned by gonadal dysfunction.

CASE V.—A.P., aged thirty-four years, who had two children, was sent from a dermatologist because of a rash on the extremities which became worse at the menstrual periods. The diagnosis was *erythema multiforme*. The patient gave a history of rheumatic fever. Other present symptoms were increasing weight, severe headache at the menstrual periods, hypomenorrhœa. All chemical and blood tests gave normal results. A course of œstrin combined with thyroid extract had no effect on the patient's general symptoms or the rash. A course of serum gonadotropic hormone in the first half of the cycle and of serum prolactin B in the second half of the cycle for three months had the following result. The rash disappeared, there was a reduction in weight, the headaches and the menstrual flow remained *in statu quo*.

Recently favourable results with this treatment have been reported in climacteric or post-castration psychoses. Dosage varies according to the effect aimed at and the demands of the particular organism. Recently I have had a successful and striking result with large doses of œstrin in a case of this nature.

CASE VI.—M.D., aged forty-nine years, who had had five children, complained of giddiness, headaches and irregularity of menstrual periods, tiredness and insomnia, and increase in weight. She had arterial hypertension, her systolic blood pressure being 170 and her diastolic pressure 90 millimetres of mercury. She was given 3,000 international benzoate units of œstrin a day for two months, and was put on a diet. At the end of that time she had no headaches, no giddiness, had lost one stone in weight, and the systolic blood pressure was 140 millimetres of mercury, the diastolic pressure being 90 millimetres.

CASE VII.—V.P., aged forty-eight years, had had four children. She was complaining of insomnia, restlessness, lack of concentration, amenorrhœa, severe headaches and flushes, and for the previous three weeks mild delusions. She was isolated and put onto bromide and "Luminal". and was given large doses of œstrin by injection, 10,000 units per day for fourteen days, and then in tablet form for five weeks. She was well enough to go back to the country after seven weeks.

This was a very striking case.

Lately it has been shown that patients with severe ovarian deficiency symptoms correspond with an increase in the urinary excretion of gonadotropic hormone, and that there is a distinct parallel between the severity of the symptoms and the level of the eliminated follicle-ripening factor prolactin A (gonadotropic hormone). For instance, when there are fifty mice units in the urine the symptoms are slight. When there are thirteen to fifteen hundred units in the urine the symptoms are pronounced (*pruritus et cetera*).

In the treatment of deficiency symptoms the dose of œstrin (folliculin) which proved most effective was that which just made the urinary gonadotropic hormone disappear and prevented its reappearance. A simple test for the effectiveness of the replacement therapy is the vaginal smear. A smear from the vaginal mucosa is taken on a glass slide, it is stained with methylene blue, and the size and number of the vaginal squamous epithelial cells are noted. A return to their normal size and shape and an increase in their number, the absence of polymorphonuclear cells, and a return of the clean appearance in the smear indicate the efficiency of the treatment.

In less severe cases twenty to fifty thousand international benzoate units weekly are necessary, and in

severe cases a hundred thousand units weekly are needed to start with. These doses may be reduced cautiously when the symptoms become less severe. To avoid glandular hyperplasia of the endometrium, however, it is advisable to determine in each case the smallest dose necessary for success.

In obstinate cases it is my practice to combine oestrin therapy with serum gonadotropic hormone in the form of "Antostab" and "Physostab", which is obtained from the serum of pregnant mares. In the near future one may expect more potent gonadotropic hormones of this nature.

Before I bring this address to a close it would be opportune to mention briefly the relation of vitamins and sex hormones, and to say a few words on vitamin deficiency in pregnancy.

A common discussion of both vitamins and hormones is justified by the recently recognized relationship between them, both from the point of view of function and chemical constitution. Both play an indispensable role in the well regulated life. Insufficiency of either in the organism produces comparable phenomena—the so-called deficiency diseases, for example, hypovitaminosis or avitaminosis when there is a lack of a vitamin, and symptoms of hormonal insufficiency when any particular hormone is absent.

The close relationship in their modes of action on organic function, too, either in cooperation or antagonism, has been described repeatedly. Best known in this respect, perhaps, is the inhibitor effect of vitamin A on the stimulatory activity of the thyreoid hormone on the metabolism, a discovery which has already been successfully tested in the treatment of hyperthyroidism. Besides this, we now know of the mutual relationship between vitamin E and the sex hormone, and between vitamin D and the parathyroid—relationships which are already finding partial expression in sterilization treatment and the therapy of tetany respectively.

Vitamins and Hormones.

Finally, there is frequently a distinct relationship between the chemical constitution of the vitamins and hormones. Several vitamins and hormones belong to the sterol group.

A few brief facts showing the importance of the recognition of vitamin deficiency in pregnancy are the following:

1. Deficiency of vitamin A produces, among other things, alterations in the visual purple, giving rise to one of the earliest and most frequent of its symptoms—so-called night blindness or nyctalopia.
2. A not uncommon and distressing feature of pregnancy is polyneuritis; this in many cases is due to a vitamin B₁ deficiency.
3. Deficiency of vitamin C may give rise to dental caries of pregnancy and bleeding gums, and possibly also to disorders of the gastro-intestinal function.
4. Deficiency of vitamin D tends to produce latent rickets in the foetus and also tetany in the mother.

5. The relationship of vitamin E deficiency and habitual abortion has recently been established.

These few brief facts show the interesting possibilities of vitamin therapy in pregnancy. The future will undoubtedly see further advances in vitamin research.

Conclusions.

In conclusion, it is hoped firstly that a clear conception of the underlying principles of the physiology of the sex hormones has been given, and that an endocrine background has been established which will enable you to read future publications on this subject with more interest. And, lastly, it is hoped that the more important and most effective methods of female sex hormone therapy have been clearly indicated.

Acknowledgements.

I wish to acknowledge my indebtedness to Professor J. Young and his staff at the London Post-Graduate Hospital; to the late Professor Dr. G. A. Wagner (Director), Professor Kaufmann and Dr. W. Rust, of the Universitäts Frauenklinik der Charité, Berlin; and to Professor W. P. Watson and his staff at the Sloane Hospital for Women, New York.

DIFFICULTIES IN THE THIRD STAGE OF LABOUR, WITH SPECIAL REFERENCE TO THE RETAINED PLACENTA AND THE MOJON-GABASTON TECHNIQUE.

By W. KEVERALL MCINTYRE, M.C., M.D., M.R.C.O.G.,
Launceston.

HAVING successfully delivered the baby, the obstetrician feels that the really important part of the work has been done, and that with ordinary good fortune he should be back in bed within the hour. Alas, how often are his hopes ill founded, and how often does he find that in the third stage of labour his troubles are only just beginning! After a difficult and prolonged first and second stage he is on the lookout for possible complications; but frequently enough, even in cases which have given no anxiety whatever before the baby was born and in which the conduct of the third stage has been above suspicion, a *post partum* hæmorrhage may occur, or there may be difficulty or delay in the expulsion of the placenta and membranes.

We may accept the usual distinction between adherent and retained placenta, the former being a placenta wholly or partly attached to the uterine wall, and the latter one that has entirely separated, but is still wholly or partly retained in the uterus. *Placenta accreta* is a rare condition that generally has to be dealt with by hysterectomy. There is no spongy layer, and as the muscle wall of the uterus is actually invaded by the villus, separation may be impossible. In some cases there are probably degrees of attachment; some of the cotyledons have

normal attachment and others invade the wall. This would explain the firm hold some part of the placenta occasionally has on the uterine wall, and the difficulty experienced in the separation of certain areas while the placenta is being removed manually. Retained and adherent or partly adherent placenta is one of the most common causes of *post partum* hæmorrhage, and I wish to discuss only a few of the many predisposing causes of either of the above complications of the third stage of labour.

The longitudinal muscle fibres must always take a little time to recover tone after the uterus has been emptied, and the more they have been stretched, the longer they will take to accommodate themselves to the new conditions. Each succeeding pregnancy leaves the muscle fibres permanently changed by a gradual replacement of fibrous tissue, which in time affects their efficiency.

Prolonged labour leads to exhaustion, especially if the patient has not been given adequate nourishment. One of the disadvantages of the use of analgesics is that it is often difficult to get the patient to take food; and if the third stage is prolonged, and especially if any manipulation such as Credé's expression has to be carried out, obstetric shock not infrequently occurs, often without any warning. It is very important to insist that glucose and other carbohydrates should be given as freely as possible during labour. Unless the necessity is emphasized, many nurses neglect this measure.

If the cause of shock is not recognized and it is thought the collapse is due to loss of blood, further efforts may be made to express the placenta or even to remove it manually, with greatly increased risk to the patient. In these cases, so long as bleeding is not excessive, the intravenous administration of glucose in saline solution should be begun at once, shock should be treated by warmth *et cetera* and the uterus should be left alone until the shock has passed off.

In our anxiety not to be meddlesome, and because of the fear of sepsis, there is, I think, a tendency these days to avoid the use of forceps and sometimes to leave the patient longer than we should in the late second stage. The more prolonged labour leads to further exhaustion and to more trouble in the third stage.

The emotional factor, which it would be out of place to deal with fully in this article, is one which has a very definite effect on labour. A number of influences increase the apprehension of many women, especially *primiparæ*, who are approaching their confinement. Increased sensitiveness to pain exaggerates sympathetic stimuli of the nerves which are the motor supply to the circular muscle fibres of the cervix. This state of tension at the outlet increases pain and prolongs labour. The muscular exhaustion which follows a long, tedious labour may lead to atony of the uterus in the third stage. to *post partum* hæmorrhage and possibly to difficulties with the placenta.

Another point which calls for consideration is the relative increase in the number of first confinements owing to the rapid decline in the size of families. In a series of articles which appeared in *The Sydney Morning Herald*, A. E. Mander⁽¹⁾ analysed the birth and death statistics of Australia. He showed that there had been no reduction in the absolute number of first and second births, the whole decrease having occurred in the number of births beyond the second. There are not fewer people who have children, but the same number of people have fewer children. Two-thirds of all married people nowadays have an average of just over half a child each, and the remaining third produce an average of two and a half children each.

Since it is with the *primiparæ* that we have most of our difficulties, I think it will be agreed that with this proportional increase in first confinements we have to expect a relative increase in our anxieties during the first and second stages and more risk of complications in the third stage. The following analysis of my last consecutive 1,000 cases is of interest (Table I).

TABLE I.
Percentage Occurrence of First and Later Pregnancies
in 1,000 Cases.

Pregnancy.	Percentage.
First	44.0
Second	26.3
Third	15.0
Fourth and over	14.7

Most British text-books on obstetrics condemn the use of pituitrin in the third stage of labour while the placenta is still in the uterus, because of the risks of hour-glass contraction, or of contraction ring of the cervix or lower uterine segment, imprisoning the placenta. Blomfield⁽²⁾ in a recent article discusses the administration of pituitary extract in the third stage of labour. He contrasts the teaching in England with that in America, where De Lee, Schumann and other well-known authorities strongly advocate the use of pituitrin extract in the third stage. De Lee,⁽³⁾ however, points out that after its use the uterus often contracts unevenly and may imprison the placenta. Blomfield carried out a series of experiments at the Leeds Maternity Hospital. He administered pituitary extract in the third stage in over one thousand cases and compared results with a control series. He stated that he had reached the following conclusions: (a) the amount of hæmorrhage was not much affected, except that it was slightly less in the cases in which pituitary extract was used; (b) the percentage of cases in which the placenta was retained for more than one hour was 0.95 in the treated, as against 1.25 in the control series; (c) there was no danger whatever in giving injections of pituitrin or pitocin in the third stage of labour. There were twenty-five cases of retained placenta in the series of 1,187 cases compared to twenty-eight cases in the control series of 1,546. He had two cases of contraction ring in each series.

My own experience with pituitrin in the third stage is limited to its use in odd cases over a few years. For a time I used it freely; but of late I use it in selected cases only, because of difficulties for which, rightly or wrongly, I blamed the injection. I am convinced that it has no useful effect whatever on the flabby, inert uterus which has to be stimulated by constant kneading to keep it from filling with blood. In such cases the greatest effects attained are irregular, localized contractions, which are of no assistance in separating or expelling the placenta, but which may imprison part of it and delay or prevent its expulsion. I have had to use manual interference on two such occasions; but, of course, there was no definite proof that the pituitrin was to blame. In moderate degrees of slackness, when the uterus is just unable to expel the placenta, pituitrin is effective and Blomfield's conclusions seem to justify its use.

We are all alive to the grave risks involved in a manual removal of the placenta, especially as it is usually carried out when the mother has already lost much blood and is suffering from a greater or less degree of shock. Personally, I view it with more apprehension than any other obstetrical or gynaecological operation.

Currie⁽⁴⁾ pointed out the dangers of too long a delay before manual removal of the placenta when *post partum* hæmorrhage occurs. Undoubtedly it is the fear of complications that encourages us to avoid a manual removal if possible, and either to persist in a hopeful waiting policy or to continue our efforts to express the placenta by Credé's method, sometimes assisted by cautious pulling on the cord. The well-known dangers accompanying manual removal, namely, rupture of the uterus, hæmorrhage, shock and sepsis, incline us to postpone the operation in the hope of avoiding it and to adopt proceedings which we ordinarily condemn as unsound.

When a portion only of the placenta has been retained, it is open to discussion whether this should be removed at once. Some obstetricians prefer to leave it alone, in the hope that ergot and pituitrin, or later vaginal or uterine douches will get rid of the retained portion. I think, however, that the majority will agree that any placental tissue left behind should be removed at once, because of the risk of infection or of severe secondary *post partum* hæmorrhage. If it has to be removed during the puerperium there is a much greater risk that infection will be set up or aggravated.

Munro Kerr⁽⁵⁾ was, I think, the first to point out that during a manual removal manipulations should if possible be performed inside the amniotic sac, so that any organisms which may be introduced will remain inside the sac and be swept away when the placenta and membranes are removed. I do not think it is always possible to do this, as often the membranes have been torn at the placental margin, or will tear when the obstetrician begins stripping with the fingers.

It is impossible to obtain reliable figures as to the frequency with which manual removal is carried out in private practice. In hospital records the figures vary from 0.5% to 1.4%. At the Rotunda⁽⁶⁾ over a large series the rate was 1%. Munro Kerr quotes the following: Strecher, 0.52%; Wagner, 1.36%; Prague, 1.2%. My own figure for the last 1,350 consecutive cases up to the time I adopted the Mojon-Gabaston manoeuvre was 1.3%. This rather high rate was due to the fact that of late I had been resorting to manual removal before the patient became desperately ill from shock and loss of blood. This increased the frequency rate, but decreased morbidity and the risks of a fatal issue.

The death and morbidity rates in hospitals are probably higher than those in private practice, since many patients are sent to hospital at a late stage in a serious or desperate condition, often after operative interference in the second stage. Currie⁽⁴⁾ quotes the Leeds Maternity Hospital death rate at 15.4% and morbidity at 45.2%.

Having discussed a few of the difficulties and dangers in the third stage of labour and their causes, I should like to draw attention to a method of dealing with one of them, namely, retained placenta, which I have been using for the past twelve months with considerable success. This method is a slight modification of the Mojon-Gabaston technique of umbilical cord injections.

After practising on a large number of freshly delivered placenta, I have adopted a technique which I consider an improvement in one or two respects on those of which I have read; I have found this technique to be of great value in practice. In many cases this manoeuvre saves a manual removal, reduces the morbidity and may definitely be counted a life saving measure.

The Mojon-Gabaston Technique.

Historical.

In looking up the literature on the Mojon-Gabaston method of assisting in the delivery of the retained placenta, I was surprised to find that in most European countries and in the United States and South America the practice has been fairly common for many years; a large number of articles have been written and cases have been reported in foreign journals. Jarcho⁽⁷⁾ describes three successful cases and gives a short historical survey which he condensed from a complete history published by Koerting in 1925. The following very brief notes are taken from Jarcho's article:

The method was first described by Mojon in 1826, who said that "water slightly acidulated with vinegar is injected with some force through the vein of the umbilical cord into the placenta, after allowing the flow and expressing of as much blood as possible from this vein by way of precaution. Whether because of the sudden pressure which the injected water exerts in the fetal placental tissue, or the cold which is immediately transmitted from the placenta itself to the placental site of the uterus, in any event, the desired expression takes place without the necessity of introducing the hand into the uterus. In case the first injection does not prove effective, a second one may be attempted after the liquid previously injected has been evacuated".

Asdrulali, of Rome, claimed to have taught his students, from 1814, that if spirits of wine was injected into the umbilical vein, the fluid penetrated to all parts of the placenta; but it is not clear that he actually used the method in practice. Other reports were made from time to time through the century, some praising and others condemning the practice. In 1829 Basedow tried it and found it of no value. In 1834 Most reported that after the birth of twins he had injected cold water acidulated with vinegar through both umbilical cord veins. This stopped the hæmorrhage, and the uterus contracted and expelled the large placenta. D'Outrepoint struck a warning note condemning the practice, as the injection of cold water "caused delay and inflammation of the uterus, and eventually degeneration". The method seems to have fallen into disuse, probably discredited by the septic infections that followed its use in pre-antiseptic days, until Gabaston, in 1914, in Buenos Aires, published a modification of Mojon's technique for dealing with retained placenta. He described his technique for injecting the umbilical vein with normal saline solution. This article revived interest in the practice. It has come into more general use in the Continental countries, and British obstetricians are now beginning to realize the value of this admirable and useful procedure.

Koerting's historical description, written in 1925, is probably the most complete record. He stated that distension of the placenta often rendered Credé's expression unnecessary, and was of the opinion that to get the best results the obstetrician should not employ the Credé manœuvre beforehand. He considered that if there had been severe hæmorrhage the injection of the cord was contraindicated. The Frankfort clinic reported 150 cases and claimed a reduction in manual removals from 4.5 to 1.5 per thousand cases. Wagner, of Prague University, claimed a 50% reduction, and considered that the Mojon-Gabaston method was destined to replace Credé's expression as well as manual removals.

Technique of Treatment by Injection.

Jarcho uses saline solution, made up when required; saline tablets are dissolved in the required amount of water and boiled and sterilized. He uses it warm, and injects by means of a "Luer" or "Record" syringe of 20 to 100 cubic centimetres capacity. He injects the needle close to the pudendum, as this part is less likely to be soiled by fæces than the distal end and because the blood here is less likely to be clotted. The needle attached to the syringe is inserted in a proximal direction into the vein parallel with its course. It is held in place with an artery clamp. If a second puncture is necessary, the first needle is withdrawn and the clamp holding it in position is tightened to prevent the return flow of saline solution through the opening. Then the second puncture is made closer to the pudendal orifice. After the needle is in its proper position, from 200 to 300 cubic centimetres of warm sterile physiological saline solution are injected slowly

into the placenta through the vein and the physician waits for uterine contraction and expulsion of the placenta. Sometimes greater and sometimes smaller amounts are required, and from ten to twenty minutes may elapse before the placenta is expelled or can be expressed by Credé manœuvre. Currie⁽⁴⁾ uses a trocar and cannula, and holds it in place with a cord. He uses a Higginson's syringe and injects sterile saline solution at blood heat as rapidly as possible. The distended placenta packs the uterus and stops the bleeding and in most cases elicits contractions forcible enough to expel the placenta. Up to the end of 1935, at the Leeds Maternity Hospital, the umbilical cord had been injected on 186 occasions, mainly for retained placenta with or without *post partum* hæmorrhage. Of these, only two cases ended fatally and eight patients were reported to be morbid. One of the patients who died was moribund on admission to hospital, and the other had advanced heart disease. The septic cases all resulted from instrumental delivery. In comparing these figures with those of manual removal, Currie states that the death rate was 1.6% as against 15.4%, and that the morbidity rate was 8% as against 45.2%. He also uses the injection as a prophylactic measure against *post partum* hæmorrhage, as a precaution in cases of *placenta prævia* immediately after delivery of the child, and as a means of clearing the field before perineal wounds are sutured.

Formerly I used to tie the usual guide ligature near the vulva, but found it difficult to get a needle or cannula into the empty collapsed vein in the cord. After several failures I adopted the practice of tying two ligatures at the distal end and cutting the cord between them when separating the baby. This prevents the cord from emptying itself and the veins remain distended and are easily injected if necessary later.

A Higginson's syringe is the most satisfactory instrument for injection, as the fluid can be injected more quickly, and this is of great practical importance. I use a "Sterilendum" enema syringe which has glass valve fittings and can be boiled frequently without deterioration. The "Record" syringe, or a large ear syringe which I tried out, has to be filled repeatedly and causes delay; also air bubbles are more likely to be included in the injection. To the syringe is attached a small bone nozzle, such as is used with an enema, filed down thinly enough to enter any cord vein and roughened on the surface to give good hold to the ligature. The distended vein is snicked with sharp-pointed scissors and the nozzle inserted and tied in with a cord ligature; the procedure is the same as that used in an ordinary intravenous injection of saline solution or blood transfusion. I sometimes use a large-bore needle; but prefer the nozzle, first, because it has a larger bore and the placenta can be more rapidly filled, and secondly, because the needle can so easily transfix the vein and cause delay.

Care must be taken not to inject air into the vein. I have not seen any reference to this danger, but

it is obviously a real one. If the end of the syringe escapes from the solution and air enters the bulb, the nozzle should be withdrawn and the syringe refilled and again inserted. Some of the villi probably actually open into the uterine sinuses, and air could be thus directly pumped into the uterine veins. We are perhaps inclined to be less nervous about an occasional bubble of air getting into the vein than we used to be when giving intravenous injections; but I should feel very concerned about the large bubbles that could be injected directly into the uterine sinuses from a syringe such as that used in the cord injection.

A second point I should like to emphasize, and one to which I have seen no reference, is the value of the injection of hot saline solution, such as is used in an intrauterine douche in *post partum* hæmorrhages. As would be expected, the muscular response is quicker and much more pronounced than when a tepid or warm solution is used.

I have found, by experimenting on freshly delivered placenta, that with an average length of cord the temperature of the solution drops 5° C. (10° F.) in the placental tissues. The injection has to be commenced at a proportionately higher temperature. In practice a temperature of 52.5° C. (125° F.) seems to give good results. If it were possible to be sure that the placental surface was intact, a temperature of 54° C. (130° F.) might be safe; but as the fluid runs through any torn surface into the cavity of the uterus, this might still be too hot for the patient.

As a rule, as soon as sufficient hot saline solution has been injected the patient complains of pain, the uterus contracts strongly and the hæmorrhage diminishes or ceases altogether. This contraction is often sufficient to expel the placenta; but if the cause of the delay is a contraction of the lower segment it may be necessary to give an anæsthetic to relax this spasm. If this is not effective, the injection may be repeated if the uterus again becomes atonic. Even if this fails and manual interference has to be resorted to, it is found that when the contraction ring has been dilated the engorged and separated placenta is very quickly and easily removed with very little shock to the patient. The ease with which this firm, compact placenta may be removed, as compared with the flabby, irregular, non-injected placenta, has to be experienced to be fully appreciated.

Dangers and Contraindications.¹

1. In pre-antiseptic days the method must frequently have been responsible for infection during the puerperium; but even that would be less dangerous than would bacteria introduced by the hand into the uterus during a manual removal. The increased hæmorrhage and shock, the risk of perforation of the uterus, the trauma to the tissues

et cetera would still further load the dice against the patient. In these more fortunate times, if proper precautions are taken, there should be no danger that this procedure would infect a patient or render her more susceptible to infection.

2. If the injection is given carelessly there may be a very real danger of an air embolus getting into the maternal veins, with possibly fatal results. If proper care is exercised, this danger should not occur. This can be easily shown by the injection of freshly delivered placenta.

3. Physiological normal saline solution only should be used. In one case I injected sterile water instead of saline solution and the patient a few minutes later complained of feeling cold and began to shiver; the attack amounted to a mild rigor. This lasted about twenty minutes, even though the room was warm and the patient had not been greatly exposed and had not suffered from shock. Forget referred to such a case, and thought it a possible contraindication to the method; but Jarcho⁽⁷⁾ pointed out that it was probably due to the fact that water was forced into the circulation through the uterine sinuses. I have not observed this effect when using normal saline solution. For the same reason, it is better not to use antiseptics in the injecting fluid.

4. Profuse hæmorrhage is considered by most writers to be a contraindication to the method; I agree that this is so—not because the injection of the hot solution will increase the hæmorrhage, for, on the contrary, it is more likely to check it. A hot douche is one of the recognized methods of combating *post partum* hæmorrhage, the hot solution stimulating contractions of the uterine muscle. It is contraindicated in more severe hæmorrhage because of the time factor. The sooner the placenta is away the better, and a manual removal is the quickest way of attaining that end. But for that, I see no real objection to the use of the method, and apart from such cases of emergency I would, and do, try the effect of injection of the cord before proceeding to the more dangerous operation.

5. A more real objection might be raised when the cause of the retention is an hour-glass contraction, or a contraction of the cervix or lower segment. By increasing the bulk of the placenta, may not the obstetrician add to his difficulty? I do not think this is so. He is often able to relax the ring by administering an anæsthetic, preferably nitrous oxide and oxygen or ethylene, or a few whiffs of chloroform. If there has not been much loss of blood, and if the blood pressure is not too low, spinal anæsthesia is very suitable for this operation, as shock is not so easily produced by it, and the uterus retracts well. In the majority of cases these conditions are not fulfilled, as the patient has probably had a general anæsthetic during the second stage. There is usually some degree of shock accompanied by lowered blood pressure, and considerable loss of blood has taken place before a manual removal is considered necessary. The administration of eight cubic millimetres of amyl nitrate, or of "Spasmalgin" (Hoffmann La-Roche), sometimes

¹ June, 1939. Since writing this paper I have had one other case of retained placenta. The third stage of labour lasted for four hours, and by the time I was called in the patient had lost a great deal of blood. The cord was not suitable for injection, as the blood had clotted along its whole length. This is the only case in which I have found this contraindication to injection of the cord.

causes a temporary period of relaxation, during which the placenta may be expressed. It is easier to express the placenta when it is engorged and firm than when it is flabby, and there is less risk of inversion of the uterus. At the worst, if a manual removal is necessary, as already stated, it is a much safer and easier operation after the cord has been injected.

My routine procedure in cases of *post partum* hæmorrhage with retained placenta is as follows. If there is hæmorrhage which cannot be controlled, I inject the cord with saline solution at 52.5° C. (125° F.) without delay and proceed to a manual removal if the hæmorrhage continues, or if the placenta cannot be expressed. If there is no hæmorrhage and the patient is in a satisfactory condition, I wait from half an hour to an hour, keeping careful control of the uterus. If the placenta cannot then be expressed, I inject the cord and if necessary repeat the injection. If this again fails, I give one cubic centimetre of pitocin or pituitrin and prepare for a manual removal under nitrous oxide and oxygen or ethylene as a rule. The placenta is usually found to have separated and is easily removed with very little intrauterine interference.

Manual Removal of the Placenta.

In an analysis of the eighteen manual removals in this series of 1,350 cases, no outstanding causes can be found for the retention; 61% were first pregnancies and 22% second pregnancies. The principle of avoidance of unnecessary interference in all stages of labour was observed. Forceps were used in 14.5% of cases, and in 90% of these low application of forceps was required with the head on the perineum. In the third stage I allow a hand on the fundus to control the uterus, and as long as there is no bleeding, rubbing or kneading is avoided. If separation has taken place, I attempt a Credé expression after thirty minutes and may repeat the attempt after forty-five and after sixty minutes if necessary.

In the eighteen cases of manual removal I had used forceps five times; in only one of these was delivery difficult. In two cases the foetus presented by the breech, and in one a podalic version was performed for slight disproportion. In some of the remaining cases the first and second stages were prolonged; but only one patient, who had early cardiac distress and who died a few hours later, gave any special anxiety until the third stage.

Pituitrin was used in five cases, and in one of these a contraction ring developed. Four patients had preeclamptic toxæmia and had been under treatment for some weeks. In ten cases the placenta had not separated and in four of these it was completely adherent and very difficult to strip off the uterus. The remaining six were only partly adherent. A contraction ring was present in four cases only.

Results.

Seven patients, or 38.8%, were febrile during the puerperium; all but two had slight pyrexia for five

to ten days only, with no further complications. Two developed pyelitis and their temperatures took longer to settle down. None of the patients had septicæmia.

One patient, a *primipara*, who was delivered of twins, had an hour-glass contraction with one placenta above and one below the contraction ring, which I found very difficult to dilate. She had preeclamptic toxæmia with hydramnios, and in the third stage had severe *post partum* hæmorrhage from the atonic uterus and suffered severely from shock. She collapsed and very nearly died, but eventually made a surprisingly rapid recovery.

There was one death.

The patient was a *multipara* with a family history of death from sudden heart failure. The foetus persistently presented in the occipito-posterior position and the patient showed signs of distress before the end of the second stage. I called in a consulting physician, Dr. Newell, and after manually rotating the head, applied forceps low and effected an easy delivery. Signs of cardiac distress continued and were aggravated by a steady uncontrollable ooze from the uterus. We manually removed the placenta under nitrous oxide and oxygen anaesthesia. It had separated and was lying partly in the vagina, nipped by a contraction ring. It was very easily removed and bleeding ceased. The patient continued to be very restless and distressed, and in spite of our efforts she died two hours later.

The last case was a manual removal after an unsuccessful Mojon-Gabaston injection of the umbilical vein. It was one of the earlier cases in which I used the method and the technique was faulty. I was not able to make a rapid injection and I did not use a hot solution. I found that the placenta had separated, and because of the injection it was turgid and very easily removed without any digital stripping.

Mojon-Gabaston Injection of the Umbilical Vein.

In all, I have used the Mojon-Gabaston method of injection of the umbilical vein in eighteen cases in which there was hæmorrhage or delay in expulsion of the placenta. In at least three of these I feel sure a manual removal would have been necessary had the injection not been used or had it failed.

The six earliest cases were complete or partial failures for one or another reason, mostly faulty technique; but the last thirteen were all successful, in that hæmorrhage was checked and the duration of the third stage was reduced; and in at least three abnormal cases a manual removal was avoided. In no case was the puerperium abnormal—a striking contrast to the after-results in cases of manual removal.

Reports of Cases.

I give brief records of five typical cases in which the Mojon-Gabaston method was used.

CASE I.—Mrs. H., a *primipara*, was aged twenty-seven years. She had a twin pregnancy. The first and second stages of labour were prolonged but uneventful. Morphine and hyoscine were used as analgesics. In the third stage the uterus was atonic and clots formed and were expressed at intervals. The uterus had to be constantly kneaded to be kept under control. Credé expressions, attempted after

half an hour, three-quarters of an hour and one hour, failed. The patient had lost in all about four pints of blood, and after preparing for a manual removal, I injected twenty ounces of hot saline solution at a temperature of 48.6° C. (120° F.) into the umbilical vein of each cord. Towards the end of the second injection the uterus contracted very strongly and both placenta and membranes were expelled spontaneously.

Had this not occurred, I should have carried out a manual removal without delay. This case is a striking contrast to the twin pregnancy quoted above, in which I had to remove the after-births manually.

CASE II.—Mrs. C., a *primipara*, was aged twenty-two years. The baby weighed 4.1 kilograms (nine pounds). The fetus failed to rotate, and after a prolonged, exhausting labour, I delivered it in the occipito-posterior position, being unable to rotate it manually. The third stage lasted one and a half hours, with intermittent bleeding from the irregularly contracting uterus. Signs of shock began to appear, and I injected the cord with 708 cubic centimetres (25 ounces) of saline solution at 48.6° C. (120° F.). The uterus immediately responded with strong contractions, and shortly afterwards I was able to express placenta and membranes complete.

This patient had lost a considerable amount of blood, and I should not have delayed much longer before carrying out a manual removal.

CASE III.—Mrs. S., a *primipara*, was aged twenty-four years. She had triplets. She had preeclamptic toxemia, and labour occurred prematurely at seven and a half months. All stages caused great anxiety; one placenta had a low implantation, and hæmorrhage continued for ten hours before the patient went into labour, more than two pints of blood being lost. Medical induction brought on labour contractions, and the patient was eventually delivered of one living and two still-born babies. During the period between the births she required intravenous injections of glucose and saline solution and blood transfusions. She had vomited during the whole of the long first and second stages, and could not retain food or fluids for more than a few minutes. The third stage was stormy, as she had obstetric shock and a flabby, atonic uterus. Five hundred and sixty-eight cubic centimetres (twenty ounces) of saline solution were injected into each of the three cords, but it was not so hot as it should have been. The uterine contractions were not strong enough to expel the placenta, and though one protruded through the vagina it could not be expressed. In twenty minutes I again injected the cords, but was unable to express the placenta any further. I then gave one cubic centimetre of pituitrin and anaesthetized the patient with nitrous oxide and oxygen. The contraction ring relaxed and I was able to express the three placenta.

But for the cord injection a manual removal would have been necessary in this case, probably with fatal results due to the increased shock and hæmorrhage.

CASE IV.—Mrs. M., a *multipara*, was aged twenty-nine years. The first and second stages of labour were normal. The baby was born before I arrived. The placenta was retained for two and a half hours. The uterus was slack, but the patient had lost only a few ounces of blood and was in good condition. I injected the cord with 420 cubic centimetres (15 ounces) of saline solution at 48.6° C. (120° F.). The uterus contracted immediately and I expressed a placenta with a large *placenta succenturiata* complete with membranes. The patient suffered no shock.

CASE V.—Mrs. F., a *multipara*, was aged twenty-seven years. The first and second stages of labour were normal. In the third stage rather free hæmorrhage began from the slack uterus, so after thirty minutes I injected the cord

with 280 cubic centimetres (10 ounces) of saline solution at 48.6° C. (120° F.), and a strong contraction expelled the placenta and membranes complete.

In the last two cases the question of manual removal did not, of course, arise, and in all probability the placenta would have been expressed sooner or later. I have quoted them to show that the method can be safely used at an early stage to control or prevent hæmorrhage and as an alternative to repeated kneadings of the uterus to stimulate contractions and Credé expressions, which so often cause shock and occasionally end in a manual removal.

Acknowledgement.

I am indebted to my partner, Dr. T. G. H. Hogg, for his assistance and cooperation in carrying out the above experiments.

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THE INTRACUTANEOUS INJECTION OF SMALL MEASURED VOLUMES OF LIQUID.

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INTRACUTANEOUS injections of small measured volumes of liquid have frequently to be made in the practice of clinical medicine, and sometimes as in the application of the Mantoux test for tuberculosis infection, the volume to be injected is very small, of the order of 0.1 cubic centimetre; yet accuracy of measurement is desirable in order that the test may be standardized. Recently there has been described a satisfactory method of carrying out the Mantoux test with a single injection,⁽¹⁾ the volume of which is 0.025 cubic centimetre.

It is not difficult to measure these quantities with sufficient accuracy with a tuberculin syringe; but if any of the liquid should escape alongside the needle, or if the subject should move and the needle should be dislodged with escape of liquid, or if by accident liquid should escape between the syringe and the needle, it becomes impossible to measure the dose accurately by reference to the scale on the syringe.

These sources of error could be avoided if the dose were measured by reference, not to the scale, but to

¹ From the Royal North Shore Hospital of Sydney Institute of Medical Research. Work carried out with the aid of a grant from the National Health and Medical Research Council.

the size of the bleb produced in the skin, provided that a constant relationship was known to exist between the volume of liquid injected intracutaneously and the diameter of the bleb produced by it; and in fact it is much easier to observe and measure the latter than the former. Accordingly experiments have been made to correlate the volume of intracutaneous injections and the size of the bleb produced. It has been found that a relationship exists between the two so close as to permit an intracutaneous injection to be measured by observation of the size of the bleb produced by it with sufficient accuracy for clinical purposes. The findings were as follows: (i) an intracutaneous injection of 0.025 cubic centimetre produces a bleb about 5 millimetres in diameter; (ii) a bleb 5 millimetres in diameter is produced by an intracutaneous injection of about 0.025 cubic centimetre; (iii) an intracutaneous injection of 0.1 cubic centimetre produces a bleb about 10 millimetres in diameter; and (iv) a bleb 10 millimetres in diameter is produced by an intracutaneous injection of about 0.1 cubic centimetre.

The clinician applying the Mantoux test should have by him when making the injection the millimetre scale and pair of dividers used for measuring the size of the reaction.

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Reviews.

A DICTIONARY OF TREATMENT.

In previous editions of his "Dictionary of Treatment", Whittle's primary aim was to place in the hands of the general practitioner a work of reference covering the whole field of medical and surgical practice. This principle has been adhered to by Allison and Calvert in preparing the eighth edition, published in 1938.¹

As stated in the preface, "procedures which are outside the scope of general practice are only referred to briefly, and attention is directed chiefly to consideration of the main principles of treatment, and to remedies which have undergone sufficient trial to render them worthy of inclusion in a dogmatic work of this kind".

It is apparent on perusal of the book that the surgery of the general practitioner—for whom this book is intended—is regarded primarily as a clearing station from which many of the more serious cases are referred elsewhere for investigation and treatment. For the average practitioner in this country this constitutes a definite limitation. The treatment of appendicitis, for example, in its various stages and of paralytic ileus—in fact, of acute intestinal obstruction in general—are too briefly discussed to be of real value to the practitioner who is actually seeing the patient through; whilst almost all the useful measures receive mention, there is too little delineation of the differing phases of illness for which these various measures are appropriate. Exactly the same may be said of the sections dealing with chronic arthritis, leucorrhœa, and, perhaps

most serious of all, acute gastro-enteritis, whether of adults or children; in this country such cases of whatever severity certainly fall within the bounds of general practice.

In refreshing contrast to the foregoing, there are complete and excellent sections detailing stage by stage the treatment of hæmorrhoids, *prolapsus ani*, varicose veins, infections of the hand, and a great many other troublesome conditions. In a few instances the authors appear to have been unduly conservative in the recognition of newer methods, as in the acute stages of gastric and duodenal ulcer, in which alkaline powders are recommended rather than adsorbents, and there is no mention of treatment by continuous drip. In the main, however, criticism may be directed not at the wealth of material which the work contains, but at the rather jumbled manner in which, in a few instances, it is exhibited.

In general, then, here is a book well worthy of its place as a work of reference. In many of the more serious conditions it will serve not as a complete guide to treatment, but as an aid to memory, requiring that he who reads already possesses a sound knowledge of the subject. Withal there will be found a vast number of everyday maladies, many of them serious and dangerous, for which the pages of this book provide a complete outline of treatment in all stages. It is safe to predict that no practitioner will fail to glean from this storehouse knowledge which is not only new but of the greatest value.

ESSAYS ON SENSATION.

THAT charming writer, Dr. Edward Guy Dru Drury, has a reputation which extends far beyond South Africa, where he is a lecturer on physiology and hygiene at Rhodes University College, Grahamstown. Sir Henry Brackenbury, in a preface to Drury's "Psyche and the Physiologists", the little volume which we now discuss, states that this author's writing reveals "great knowledge and skill, much wisdom, profound sympathy and understanding, complete sincerity, and high character". As all who have read Dr. Drury's previous volume, "Choosing a Wife, and Other Essays", will agree, the author, in addition to these attributes, possesses a wide knowledge and a deep appreciation of literature, which he applies with telling effect in his own books.

The essays in the present volume, though they vary much in subject-matter and manner, have this in common—that they deal in a style which is easily comprehended with problems of psychology and of sensation. They constitute a skilful exposition of the gospel that purely physical conditions exert a tremendous influence upon mental states. The essay entitled "Labels and Luggage" is evidence of the writer's piercing discernment of the factors governing the unfolding of the child mind, and the contribution "What Do We Think With?" is a fine summary of diverse aspects of cerebral function. Perhaps Dr. Drury is at his best in the thirteen-page discussion called "Growing a New Claw". In these pages he sets down his experiences after sustaining a wound on the hand which became infected with streptococci contained in a sample of cerebrospinal fluid. Dr. Drury possesses the rare faculty of viewing his own unenviable lot, during this catastrophe, in a purely objective way. Here was an accident which may well have caused the gravest anxiety both to the patient himself and his medical attendants; but he discusses the whole affair with the cool and unemotional detachment of an onlooker at the game of chess. From the reader's viewpoint, this sang-froid greatly increases, by its very economy in words and absence of emotionalism, the effect of terrible strain during an incident which might well have involved the loss of a limb or of life itself.

If there be any fault in Dr. Drury's mode of setting down his thoughts on a very difficult subject, it lies in an occasionally laboured hunt after colourful metaphors.

¹ "Whittle's Dictionary of Treatment, Including Medical and Surgical Therapeutics", by R. S. Allison, M.D., M.R.C.P., and C. A. Calvert, M.B., B.Ch., F.R.C.S.I.; Eighth Edition; 1938. London: Baillière, Tindall and Cox. Demy 8vo, pp. 1292. Price: 30s. net.

² "Psyche and the Physiologists, and Other Essays on Sensation", by E. G. Dru Drury, M.D., B.S., D.P.H.; 1938. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 112. Price: 5s. net.

These sometimes seem to miss the mark, and analogies crop up here and there which smell a little of the lamp. The anecdote on page two, which is written in what many readers accept as Americanese, might well have been omitted; it is sadly out of keeping with the general excellence of Dr. Drury's style.

VEINS.

DR. K. J. FRANKLIN has attempted to summarize for the benefit of English readers the extensive literature which has appeared on the venous system, and to embody in it the results of his own researches. As this literature has important bearings upon physiological, pathological and clinical problems, and since the author has succeeded so well in his task, it fills a distinct need and will remain for some time the standard work on the subject.¹

After a very clear and concise account of the embryology of veins, written by K. Richardson, a very detailed account is given of the general histology of veins and the histology of special veins, including the recent research on the nerve elements. This is followed by a very informative chapter on valves, in which the historic lines of Bardeleben are shown to be untenable in the light of more recent research.

The section on blood depots and the relative proportion of blood held in reserve in different conditions is a well written account of recent researches, following the epoch-making discoveries of Barcroft.

A very large section is devoted to the veins in their relation to the nervous system, and includes an account of reactions to certain chemical stimuli. The various mechanical factors affecting the circulation of the blood in the veins are fully treated. This section includes a consideration of the factors of the contraction of muscle and of respiration.

The final chapters are devoted to a consideration of the application of the fundamental facts of anatomy and physiology to clinical problems and the application of various photographic techniques to research on the venous system, such as cinematography, radiology and infra-red photography.

As the author states, he has "attempted to show what is permanent in our knowledge of veins, to indicate where additions of value are even now being made to it, and where information about certain aspects of it are changing in the light of fresh research". There is no doubt that he has achieved his purpose, and so has provided not only a valuable work of reference, but a source of inspiration to those working in this field of research.

PSYCHOPATHOLOGY.

In "Clinical Studies in Psychopathology", Dr. H. V. Dicks, who claims to be an eclectic analyst, gives us the fruits of his experience in the investigation of the psychopathology of the neuroses.² His guiding principle has been to link up what he has observed in the process of psychotherapy with the mental phenomena of the early childhood of his patients.

As an unattached analyst, Dr. Dicks feels that he is less prone than the Freudians to extract statements from his patients which are most in keeping with the analyst's views. Throughout his work he has endeavoured to approach each case with an attitude of intellectual neutrality. At the same time he does not hesitate to bring back the patient's associations to the dominant symptom whenever analysis seems to drag or drift. In his own

words, his therapeutic procedure consists of a "painstaking working through of infantile experiences, whether real or phantastic, and their emotional contents".

In the author's experience dreams related at the beginning of treatment most often present "admirably condensed summaries of the entire psychopathology of the patient's illness". Various chapters deal with the clinical varieties of neurosis, and with sexual abnormalities and drug addiction. A chapter on ambivalence is especially interesting. Here Dr. Dicks discusses the play of opposites and the attempt to achieve unity by the elimination of the sense of hate and frustration experienced in infancy.

With regard to perversions of the sexual aim, the author produces evidence that at their roots they are feelings and phantasies of the deprivation of love, fused with the hatred thereby provoked. Exaggerated sexual impulses appear as reactions to deeper feelings of deprivation and loss of the mother. Dr. Dicks admits that it may be a task of years of analysis to free the libido from its early fixations.

Drug addiction is regarded as a fixation at and regression to the oral level of development. The link between alcoholism and homosexuality is shown by various customs and ceremonials which are often performed with a sense of guilt. Dr. Dicks suggests that morphine addiction arises out of a sense of rebellion; hence the urge to take a forbidden drug.

In the concluding chapter the author gives his evidence for the existence of three instincts—the self-preservative, sexual and aggressive, the last mentioned corresponding to the Freudian death instinct. Infantile fear is the root of repression, and the essence of psychotherapy is the restoration of a sense of security for the expression of the instinctive life. In the author's word, "every patient with mental illness was more afraid than he could tolerate when he was a baby, and the faults of his psychic structure represent the gallant attempts to allay the intolerable feeling by the inadequate means at his disposal."

The book ends with a discussion of the mind-body problem in which the author favours the concept of psychosomatic unity. This work, in which the practical experience of the author is the main content, will prove of great interest to those who practise analytical therapy and indeed to all senior students of psychopathology.

YAWS.

COMPLETE with a full bibliography, one of the most important parts of the book, Chambers has written an easily readable and interesting book on yaws.³ His data are gained from experience in Jamaica, but his conclusions apply equally well to any part of the tropics in which the disease is endemic.

Quite rightly, Chambers lays great stress on the importance of predisposing factors—humidity and rainfall, poverty, overcrowding and poor sanitation, and, most important of all, diet. As with all tropical diseases, this question of lowered resistance owing to deficient diet is urgent, as the majority of races resident in tropical areas regard quantity as of greater importance than quality.

The chapter on symptoms and course of the disease gives a full description of the lesions, which are illustrated with a group of photographs. That on differential diagnosis, written "for sanitary inspectors, nurses etc.", is perhaps a little too full and liable to lead in the non-medical mind to some confusion. Treatment, however, is described adequately, and gives concisely the modern views on the method and extent of treatment necessary, while laying stress on the importance of prophylaxis.

One grows tired, while reading, of the recurring absence of distinguishing adjectives in the text; but the book gives an interesting and full review of the author's subject.

¹ "A Monograph on Veins", by K. J. Franklin, D.M., M.R.C.P.; 1938. London: Baillière, Tindall and Cox. Super royal 5vo, pp. 432, with illustrations. Price: 27s. net.

² "Clinical Studies in Psychopathology: A Contribution to the Aetiology of Neurotic Illness", by H. V. Dicks, M.A., M.D., M.R.C.P.; 1939. London: Edward Arnold and Company. Demy 8vo, pp. 248. Price: 12s. 6d. net.

³ "Yaws (Framboesia Tropica)", by H. D. Chambers, M.B., Ch.B., with a foreword by D. Wilkie, O.B.E., M.D., F.R.C.S., F.A.C.S.; 1938. London: J. and A. Churchill Limited. Crown 8vo, pp. 193, with 15 illustrations. Price: 5s. net.

The Medical Journal of Australia

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All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE MEDICAL PROFESSION OF AUSTRALIA AND WAR: EMERGENCY PREPARATIONS.

A FEW months ago the members of the medical profession throughout Australia were asked by the Commonwealth Defence Department to reply to a questionnaire; they were asked whether they would be willing to serve the State in the event of war, and in what capacity; other particulars were also sought. Since then, apart from an isolated statement in the daily Press that certain replies had been received, no official information has been made available to the profession of what the defence authorities had in mind and what arrangements would be adopted to provide medical services to the army and the civil population if war came to Australia. Not a little impatience was manifested by some members of the profession, for they could not forget what appeared to them to be the inexcusable delay shown by the Defence Department in sending abroad for purposes of study its one and only full-time permanent army medical officer, the Director-General of Medical Services, Major-General R. M. Downes. It was only after repeated repre-

sentations had been made to the Minister of Defence by the Federal Council of the British Medical Association in Australia, backed by the publicity given in this journal to the requests, that the Defence Department decided to give the Director-General of Medical Services an opportunity of seeing for himself the modern improvements overseas in army medical organization and equipment, that he might adapt them to Australian conditions and requirements. The medical profession of Australia served with distinction in the Great War. The profession of today, like all other sections of the community, desires an honourable peace; but it would be just as ready to serve today as it was in 1914 should the dread calamity of war overtake the British Commonwealth of Nations.

From the Acting Director-General of Medical Services, Colonel W. W. S. Johnston, we have received a statement setting out the present position of the defence medical services and the arrangements recently made. We are grateful to the Acting Director-General for this statement, for we hold that information regarding emergency defence medical arrangements should come to medical practitioners through their own journal and not through the lay Press. Colonel Johnston points out first of all that the Australian Army Medical Corps consists of two main groups, the active list and the reserve of officers. The former comprises medical officers serving with the army on the peace establishment as at present, headed by the Director-General of Medical Services (D.G.M.S.). Certain positions are designed for administration and control under the D.G.M.S. at army headquarters, such as those of assistant directors of medical services (including a dental officer and a director of hygiene). In each military district (or State) there is a deputy director of medical services (D.D.M.S.), and as senior medical officer in each division there is an assistant director of medical services (A.D.M.S.). The D.D.M.S. is responsible in general for Army Medical Corps administration and training within his district. Under him are the officers allotted to the various units, such as field ambulances, divisional hygiene

sections, and so forth. One very important unit is made up of the regimental medical officers of combatant units. Recently a certain number of casualty clearing stations have been added to the establishment, positions thus being created for medical officers in these important units. The number of officers serving in these various capacities under peace-time conditions is approximately four hundred. On mobilization these numbers would, of course, be considerably augmented. The Reserve of Officers comprises in the main those who have, by reason of age or at their own request, been transferred from the active list. There is another class: medical practitioners who are granted honorary rank in the Military Forces by virtue of their professional qualifications. This reserve has been greatly increased as a result of the recent *questionnaire*; this reserve, moreover, forms the supply from which personnel will be drawn to supplement the numbers on the existing active list.

The Acting Director-General points out that in view of methods of warfare that have come into existence it is plain that casualties will not be confined to the armed forces. In order that the civil population, equally with the army, should be adequately served by doctors, there was created a body known as the Committee on Coordination of the Medical Services in respect of the civil, naval, military and air force requirements in time of war. This committee consists of the D.G.M.S. as chairman, the Director-General of Health, the Director of Naval Medical Services, the Director of Army Mobilization and two representatives of the British Medical Association in Australia. The main duties of this committee are to examine and report on the coordination of medical arrangements, including medical personnel, medical equipment and hospital accommodation in time of war, having regard to the needs of both the armed forces and the civil community. One important result of the deliberations of this committee was the *questionnaire* sent to all medical practitioners. From the information gained by this *questionnaire* a central card index has been instituted. In order that the detailed work of the committee should be carried out effectively, State committees have been formed in each

State, and these work under the direction of the central committee. In general, State committees are composed of the D.D.M.S. as chairman, two representatives of the State Branch of the British Medical Association, a representative of the State Health Department and a representative of the hospital authority (in States in which the hospital administration is not under the control of the Health Department). The amount of work devolving on these committees is great and time-consuming. The importance of careful planning in regard to preliminary organization cannot be over-emphasized; the difficulties of keeping in their proper perspectives the relationship of the needs of the army and the civil community are obviously considerable. Further than this, committees have been formed by certain State governments to deal with the protection of civilians in the event of air raids. Such plans envisage first-aid posts distributed through the larger cities and staffed by a certain number of medical practitioners. The position is summarized by the Acting Director-General of Medical Services as follows:

1. The Australian Army Medical Corps is fully staffed, and medical officers are allotted to their respective units, comprising those in the Field (*e.g.*, Field Ambulances), those on the Lines of Communication (*e.g.*, Casualty Clearing Stations and Ambulance Trains) and those at the Base (*e.g.*, General Hospitals and Convalescent Depots).
2. Civilian Medical Practice has been safeguarded by so arranging that in all districts there is maintained the proper ratio between those willing to serve in the Defence Medical Services and those willing to give medical attention to the civil population.
3. Hospital accommodation has been allocated, bearing in mind the needs of the civil community and the Army, particularly in relation to the casualties that might be expected in each of these during the early stages of mobilization.
4. Ambulance transport has received much consideration. The available number of civil and military ambulances is accurately known. Arrangements have been made whereby these may be quickly supplemented by the conversion of commercial vehicles into improvised ambulances.
5. Medical equipment has been the subject of exhaustive inquiry and thorough planning. A special subcommittee of the Central Committee has considered many aspects of the problem, including the maintenance of such essentials as drugs, surgical instruments and X ray apparatus. The result of the recommendations of this subcommittee has been the provision in Australia of drugs ordered overseas to the value of some £70,000.

5. The St. John Ambulance Brigade Overseas and the Red Cross Society, which jointly provide the Voluntary Aid Detachments as essential auxiliaries to the Defence Medical Services, have greatly extended their activities and increased their numbers.

7. Cooperation has been established between the profession and certain State Governments in regard to civilian casualties in the event of air raids.

The information supplied by the Acting Director-General of Medical Services is of importance not only to the medical profession, but also to the general public, who will realize that the Defence Department has not been idle in its preparations to meet a possible national emergency from a medical point of view. The medical profession has no wish to embarrass the Defence Department in the planning of its arrangements, but it will welcome further detailed information as the general scheme already outlined is elaborated.

Current Comment.

THE SO-CALLED HÆMOLYTIC ANÆMIAS.

DURING the past few years a series of brilliant investigations have given us a satisfactory understanding of Addisonian pernicious anæmia, of the conditions necessary for normal blood formation, and of the mode of action of the replacement therapy which is so specific. We have, too, a reasonable insight into the cause and treatment of the deficiency anæmias. O. H. Perry Pepper¹ observes that as yet no corresponding progress has been made in the anæmias which result from erythrocyte destruction—the so-called hæmolytic anæmias. These various anæmias are grouped together because of a belief that they result from increased blood destruction, although they may differ widely in the mechanism and location of that destruction, for the group includes acholuric jaundice, sickle-cell anæmia, the erythroblastoses of the newly born, as well as many forms of acute anæmia due to sudden intense hæmolysis. We have learned a little about the process of hæmolysis itself, of the relation of the reticulo-endothelial system to erythrocyte destruction, and of the cycle of pigment metabolism; but our knowledge of the details of erythrocyte destruction is incomplete. Not so very long ago pernicious anæmia was defined as a hæmolytic anæmia, with abnormal red cell formation. Pepper recalls that some patients suffering from the more "hæmolytic" types of pernicious anæmia did actually seem to benefit from splenectomy. Recent observations by Rhoads at the Rockefeller Institute tend

to place emphasis on the hæmolytic aspect of this disease.

Pepper believes that the classification of anæmias is not so distinct as is commonly supposed. In using the terms pernicious anæmia, dys hæmopoietic anæmia, deficiency anæmia, aplastic anæmia on the one hand, and the term hæmolytic anæmia on the other, we are naming only what we believe to be the chief but possibly not the only factor in the pathogenesis of any one form. Disturbances of production, either in quality or in quantity, will result in increased destruction, while increased destruction will result in increased or disturbed erythropoiesis. So each type of anæmia may disturb both functions of what Krumbhaar named the "hæmolytotoxic" system. There appear to be three methods of red cell destruction: phagocytosis by the cells of the reticulo-endothelial system, especially in the spleen, destruction by the action of some hæmolytic agent or condition of the plasma, and dissolution by simple wear and tear. The third process is normally the fate of red cells. Best states that approximately a billion erythrocytes wear out every minute. Normally there is some phagocytosis by the splenic cells and the other cells of the reticulo-endothelial system; but this is believed to affect only the worn-out erythrocytes. The spleen has been called the graveyard but not the slaughter-house of the erythrocyte.

Pepper observes that the study of hæmolysis both *in vivo* and *in vitro* shows that it may take place in a number of ways. It is not always as simple as the hæmolysis produced by hypotonic saline solution. Chemical hæmolysins, specific hæmolysins (such as are produced by an incompatible blood transfusion), toxic substances, parasites, bacteria, all act in a variety of ways in their destruction of the red blood corpuscle. Pepper gives a detailed list of the so-called hæmolytic anæmias classified according to the nature of the hæmolysis. Although their causes vary, this author observes a remarkable constancy in three manifestations common to the entire group. These are simply (i) the immediate evidences of the increased blood destruction, (ii) the compensatory hyperplasia and hyperactivity of the reticulo-endothelial system, and (iii) the evidences of regenerative action of the hæmopoietic blood-producing tissues. Another feature common to many but not all of these anæmias is the presence of a strong familial or hereditary tendency. Hæmolytic ictero-anæmia ("acholuric jaundice") and sickle-cell anæmia are the familiar examples of this; but the erythroblastic anæmias of infancy and Cooley's anæmia of infants of Mediterranean stock seem to show a familial tendency, though no true hereditary tendency is recognized.

Pepper mentions what is known of the bone marrow and bone changes in hæmolytic anæmias, but he asserts that there is little to be gained by examination of the bone marrow in these conditions. He concludes by apologizing for the fact that his paper is destructive rather than constructive. His destructive criticism, however, is rather of the

¹ *Annals of Internal Medicine*, December, 1938.

nature of a clarification of the subject. His clear and simple presentation, his avoidance of hasty judgements and unwarranted assumptions, are typical of the type of study which comes from Philadelphia, Pennsylvania.

UNRECOGNIZED HYPOTHYROIDISM.

G. K. WHARTON considers that hypothyroidism, in a mild or masked form, differs so materially from cretinism and myxedema that perpetual vigilance is required to detect its varied manifestations.¹ It is well known that iodine metabolism is closely associated with thyroid function. Three chemical compounds, iodothyroglobin, diiodotyrosine and thyroxine, have been isolated from the thyroid gland. Thyroxine prepared from the gland is itself optically inactive, but dextrothyroxine and laevothyroxine have been formed. Thyroxine in many details satisfies the requirements of the active principle of the thyroid gland, but some clinical observations give rise to the impression that the two are different. It is suggested that desiccated thyroid is more complex and gives rise to more bodily changes than thyroxine. The cells lining the acini of the gland absorb iodine from the blood and convert it into diiodotyrosine and protein combinations. As Wharton remarks, simple goitre is a response to iodine deficiency, absolute or relative. The amount of hyperplasia is inversely related to the iodine content of the gland. When hyperplasia terminates in exhaustion atrophy the gland is almost devoid of iodine. In goitre districts most of the people have an enlarged thyroid gland. This indicates that at some time there has been iodine deficiency. If further demands are made upon the depleted gland, further hyperplasia or an exhaustion atrophy may supervene unless enough iodine is supplied.

The main function of the gland is to regulate the speed of the metabolic processes of the body. The thyroid hormone acts as a catalyst, sensitizing the body cells to sympathetic stimulation. The thyroid gland acts with the suprarenals and sympathetic nervous system. The sympathetic and parasympathetic systems being antagonistic, the activity of an organ or of the whole body depends on which system is the stronger. Thyroid activity accelerates the sympathetic system, and accordingly most of the manifestations ascribed to hyperthyroidism are evidences of sympathetic over-activity. In hypothyroidism the parasympathetic system is generally predominant. The consumption of oxygen is augmented by the action of the thyroid on the sympathetic, and the tachycardia of hyperthyroidism is due to sympathetic sensitization in the cardiac centre in the brain as well as in muscle fibres. Wharton further states that the thyroid hormone furnishes the skin a sufficiency of water, fat and blood in addition to regulating the activity

of the sweat glands. Hypothyroidism or increased vagus activity causes hypersecretion and hypermotility, and these in turn explain manifestations of spastic colon, mucus in the stools, flatulence and constipation unless they are prevented by other influences. It is a common observation that mental activity is quickened by thyroid gland; but excessive mental activity is considered to precipitate hyperthyroidism. Metabolism of proteins, fats and carbohydrates as well as gaseous exchange and water balance are enhanced by the thyroid hormone. The extract of the gland gives rise to an increased rate of cell differentiation, as contrasted with the pituitary, which hastens cell multiplication. Wharton considers that anaemia in hypothyroidism is probably due to diminished oxygen consumption with a consequent decrease in the necessity for the red cells to carry this gas. The interrelations of the thyroid with other endocrine glands may be complementary or in opposition. It is now a commonplace of our knowledge that in the pituitary gland there is produced a thyrotropic hormone by which thyroid activity is enhanced, with resulting hyperplasia, increased metabolism, excretion of calcium and creatinine and a higher level of blood iodine. The thyroid has a reciprocal influence on the suprarenals and gonads, which may be direct or indirect through the pituitary. The enlargement of the thyroid gland during puberty, menstruation, pregnancy and the climacteric are known to be due to increased demands made upon it at those times. The suprarenal cortex has an inhibitory effect on the gonads as well as on the thyroid. Thymic activity is enhanced by the thyroid. The action of insulin is antagonistic to the thyroid hormone, and this may be due to sympathetic stimulation or to increased glycogenolysis. On account of their opposite actions on the sympathetic nervous system the thyroid and parathyroid glands are antagonistic. The thyroid causes loss of calcium and phosphorus from the bones, but does not produce increased quantities in the blood, as is seen in hyperparathyroidism. These substances are lost by way of the faeces and urine.

Wharton considers that certain manifestations should suggest hypothyroidism. But not all of these manifestations are found in any one case. He considers that menstrual disorders, fatigue and gastro-intestinal derangements are the most common. The menses are often irregular and generally profuse. The blood oestrogen, estimated just after the menstrual epoch, is usually excessive. Sterility and miscarriages are suggestive. Emotional derangements are common. Patients use up their energy rapidly, with resultant weakness. The appetite is generally poor, and flatulence with spastic constipation is common. Less common are migrainous headaches, drowsiness or, on the contrary, undue alertness and excitability. The skin is dry, with a tendency to crack. Eczema and acne are included amongst the manifestations, as are also dry, brittle hair and the loss of the outer third of the eyebrows. One finds difficulty in

¹ The Canadian Medical Association Journal, April, 1939.

reconciling the greasy skin of acne with the dry, harsh skin of hypothyroidism, and we are inclined to consider that Wharton unduly labours his subject. He is on sound ground when he states that underweight is as common as obesity. He considers that anaemia is infrequent and that reflexes with slow extension are characteristic findings, but that they are rarely elicited. Wharton explains the laboratory procedures for the estimation of thyroid activity. He considers that estimation of the basal metabolic rate is subject to intrinsic as well as extrinsic errors. Thyroid activity influences the blood cholesterol, so that this is high in hypothyroidism and low in hyperthyroidism. In many cases of hypothyroidism blood oestrogen is present in excessive quantity, even after the conclusion of menstruation. Oestrogen excess has also been found in men who are hypothyroidic. Wharton considers that the best diagnostic criterion of hypothyroidism is the patient's response to the exhibition of thyroid gland. He states that the possibility of hypothyroidism should never be overlooked. Even if we do not accept his contentions in their entirety, his contribution is important.

THE NUTRITIVE VALUE OF WHEAT FLOUR AND BREAD.

"MAN cannot live by bread alone." That statement is as true today as when it was uttered by divine lips many centuries ago; and modern nutritional science reiterates the claim. Nevertheless, bread, throughout the ages, has been the symbol for food, and since the latter part of the eighteenth century bread made from wheat germ flour has been the staple food of English (and Australian) people. Among the poorer classes, owing to its high calorie value and relatively low cost, it has become the chief constituent of the diet. During the past thirty years a large number of investigations have thrown light on the nutritive quality of bread, and a recent report of Copping¹ reviews our present knowledge of the problem.

Bread consists essentially of flour and water, charged with carbon dioxide as a result of action of leavening agents, and baked. Its nutritive value depends principally on the flour used in its preparation, and the question of the extent to which various degrees of milling affect this from a nutritional standpoint is of particular importance. Experience indicates that the process of milling does not seriously affect the protein or the carbohydrate content of the flour, but it does appreciably reduce the fat, ash and vitamins present. Although the proportion of protein is not greatly altered, there is evidence that the nutritive value of the protein of whole wheat is superior to that of the protein of various flours milled from it. There is evidence, too, that the carbohydrate of bread made from whole

wheat is more readily absorbed than that of bread made from white flour.

The process of milling seriously affects the ash content of flour. The removal of wheat bran and wheat germ in the preparation of white flour effects a reduction in mineral content to about one-half for calcium, one-fourth for potassium, one-fifth for phosphorus and one-fifth for iron. The loss of iron is of particular importance, since Rose and her co-workers in America have shown that iron present in whole wheatmeal is well absorbed and is efficiently used in the regeneration of haemoglobin.

An examination of white bread reveals that it contains only about one-fourth to one-sixth as much thiamin (vitamin B_1) as wholemeal bread, and investigation has also shown that whole wheat flour contains approximately twice as much vitamin B_2 as that prepared from white bread. This difference assumes special significance in low cost diets, where bread is the main source of calories. In these diets white bread cannot be expected to supply more than one-third of the daily requirement of vitamin B complex. Wholemeal bread, on the other hand, is capable of supplying the total requirement.

Vitamins of the B group are found chiefly in the germ and in the bran of the wheat grain, and to a much less extent in the endosperm. The germ has also important nutritive qualities on account of vitamin E . The fat of the germ is rich in unsaturated fatty acids; linoleic, which Burr and Burr¹ have shown to be essential for normal growth and reproduction in rats, constitutes 44% and linolenic 11% of the total fat. The needs for essential fatty acids are still unknown; but if, as seems probable, they are important for human nutrition, rejection of the germ involves loss of an important source. Further, although the vitamin E content of wheaten flour and bread has not yet been investigated experimentally, it is worthy of note that since wheat germ is one of the richest known sources of vitamin E , the removal of this constituent during the milling process must considerably lessen the nutritive value of the flour.

It is quite clear from the evidence collected in the course of Copping's review that the change-over from wholemeal to white flour that took place when steel roller mills were introduced nearly seventy years ago has resulted in the reduction of the nutritive value of the protein, in serious lowering of the content of calcium, phosphorus and iron, in reduction of the vitamin B_1 and vitamin B_2 complex content and probably in complete removal of vitamin E , all representing dead loss nutritionally. In order to change back to wholemeal it is necessary to alter the tastes of the people, to overcome the vested interests in the existing milling industry, to find a means of using wholemeal flour more quickly and of storing it more satisfactorily. The advantages to be gained in national health would make it well worth while to overcome these difficulties.

¹ *Nutrition Abstract and Reviews*, January, 1939.

¹ *The Journal of Biological Chemistry*, Volume LXXXVI, 1930, page 587.

Abstracts from Current Medical Literature.

THERAPEUTICS.

Cold Vaccines.

H. S. DIKHL, A. B. BAKER AND D. W. COWAN (*The Journal of the American Medical Association*, September 24, 1938) record the results of a study of the effects of vaccines given subcutaneously, intramuscularly and orally for the prevention of colds. Students particularly susceptible to colds were selected; control groups were studied each year and were given placebos so that they all thought they had received vaccine. The number of colds lasting more than twenty-four hours was recorded for each subject. Vaccine containing 0.015 milligramme of pneumococci, 0.015 milligramme of streptococci, 0.01 milligramme of *Bacillus influenzae*, 0.0025 milligramme of *Micrococcus catarrhalis*, and 0.0075 milligramme of staphylococci, in which the organisms were destroyed mechanically instead of by heat, was given subcutaneously; 0.5 cubic centimetre was injected every two weeks during the autumn, winter and spring. The control groups were given normal saline solution in the same way. The results showed a pronounced reduction in the number of colds *per annum* in both the experimental and the control groups. This reduction in frequency of colds was 25% greater in those who had been inoculated with vaccine. Vaccines containing similar organisms were given orally to groups of students with similar results to those recorded above. Further, a streptococcus vaccine supplied by E. C. Rosenow was given by mouth to 154 subjects, for whom there were 203 controls. It was found that an equal reduction in the frequency of colds occurred in all. The authors concluded that except for a reduction of 25% in the number of colds among those who received vaccine subcutaneously (and this percentage they regarded as valueless), vaccines did not reduce the liability to colds.

Intravenous Alimentation.

R. ELINAN AND D. O. WEINER (*The Journal of the American Medical Association*, March 4, 1939) discuss intravenous alimentation with amino-acids. Under certain conditions the intravenous administration of food is necessary; as a rule dextrose and saline solution are given. The administration of protein in the form of hydrolysed amino-acids may be indicated in nutritional oedema due to hypoproteinemia. This state may develop when insufficient protein is ingested. The authors used a 10% solution of amino-acids obtained from the acid hydrolysis of casein; this was passed through a sterile Seitz filter

directly into a 5% or 10% dextrose solution. Each litre contained about 20 grammes of amino-acids to 80 grammes of dextrose. If given slowly over the course of two hours the amino-acids were not excreted unchanged in the urine, and no objective reaction was produced, except slight feelings of warmth or chilliness. One child had a transient rash and vomited a little. About 20 patients were given amino-acids intravenously, and to eight of these large amounts were administered. Three patients had inoperable carcinoma of the stomach or oesophagus and could not be fed by mouth; three others had nutritional oedema associated with hypoproteinemia. One patient received each day for one month 4,000 cubic centimetres of a 10% solution of dextrose, containing 20 grammes of hydrolysed casein, to which tryptophane and cystine and 750 cubic centimetres of physiological saline solution were added. His general condition improved very much. Another patient, suffering from nutritional oedema associated with intestinal obstruction, gradually lost his oedema coincidentally with this treatment. The authors point out that this work was largely experimental and advise further investigations.

Thiocyanate Therapy in Vascular Hypertension.

THE work of Barker on blood cyanate levels and cyanate clearance tests stimulated E. Massie *et alii* (*The New England Journal of Medicine*, November 10, 1938) to try this method of treating hypertension in spite of their earlier unfavourable experiences. The objection to thiocyanate is that toxic manifestations often appear suddenly and without any relation to the daily or total dosage. It has been demonstrated that the varying reactions to the drug in different individuals is due to their varying ability to clear the blood stream of cyanate; further, it is possible to control the blood level of cyanate and therefore prevent toxicity, at the same time achieving useful clinical results. Fourteen patients with uncomplicated vascular hypertension were selected for treatment. All earlier methods of therapy were discontinued for three months; during this time observations were made of the patients' symptoms and blood pressure. There followed a test period during which a 5% solution of sodium thiocyanate in syrup of wild cherry was given orally; a commencing dose of 0.8 to 0.6 gramme was given on the first few days, subsequent and maintenance doses being determined by the blood cyanate level, the optimum being five to seven milligrammes *per centum*. An average daily dose of 0.2 to 0.4 gramme was found to be necessary to maintain this concentration in the blood. The treatment lasted for three months; after this there followed a further

control period of three months, during which the patients received the syrup alone, being unaware of any change of therapy. Symptomatic improvement occurred in almost every case, particularly as regards the headache or sense of fullness in the head; it was found that this was either completely banished or greatly diminished in frequency or intensity. Striking sedative effects were felt; vertigo and nervousness were well controlled and insomnia was much relieved. Excitement was well borne. Symptoms which had been relieved during the thiocyanate administration period gradually returned during the second control period. An average fall in the systolic blood pressure of 66 to 21 millimetres of mercury, and in the diastolic pressure of 33 to 8 millimetres, was observed during treatment. Toxic symptoms observed were occasional episodes of transient weakness and attacks of mild epigastric distress; nausea and vomiting occurred in one case, and three attacks of *angina pectoris* in another. No changes in the blood or kidneys were demonstrable as a result of the treatment. It seems fair to conclude that sodium thiocyanate is effective in lowering the blood pressure and alleviating the symptoms of patients with uncomplicated vascular hypertension.

"M and B 693" or Sulfapyridine.

THE Council on Pharmacy and Chemistry of the American Medical Association has adopted the non-proprietary name "sulfapyridine" for the drug 2-(para-aminobenzene-sulphamido) pyridine. This drug is marketed in Great Britain under the name of "M and B 693" (*The Journal of the American Medical Association*, February 11, 1939).

Sulphanilamide Poisoning.

H. A. SHECKET AND A. E. PRICE (*The Journal of the American Medical Association*, March 4, 1939) describe a case of fatal granulocytopenia following the administration of sulphanilamide, and review nine cases of fatal granulocytopenia due to sulphanilamide. In the case reported pulmonary embolism occurred after a hernia operation; pneumococci were found in the sputum, and sulphanilamide was administered, 8.0 grammes followed by 1.3 grammes every four hours for fifteen days. Nausea and vomiting occurred. After the fifteenth day the polymorphonuclear cells steadily diminished in number to zero, the total number of leucocytes fell to less than 1,000 per cubic millimetre, and ulcers of the mouth and tongue occurred. Blood transfusions, liver extract (two cubic centimetres twice a day) and ten cubic centimetres of "Pentnucleotide" one to three times a day, were given without effect. The patient died. Necropsy revealed embolism of the liver branch of the right pulmonary artery, pronounced congestion of the liver, spleen and

kidneys, yellow fatty bone marrow with absence of granulocytes, and ulceration of the mouth, tongue and œsophagus. Nine other fatal cases following the administration of sulph-anilamide have been reported. The *post mortem* findings have been similar in all cases. The doses given varied between 35 and 60 grammes, and were given over periods ranging from fifteen to thirty days. The authors consider that the quantity and prolonged use of the drug were the important factors in causing toxic symptoms, and that idiosyncrasy was not the cause of death. They state that if the drug yields no definite results in four to seven days its use should be suspended, temporarily at least. Toxic symptoms are very common. Cutaneous eruptions, hyperpyrexia, jaundice, a gradual fall in the number of erythrocytes and in hæmoglobin value, or an abrupt rise or fall in the number of leucocytes are indications that administration of the drug should be suspended for a few days at least.

NEUROLOGY AND PSYCHIATRY.

Pick's Disease.

IRA C. NICHOLS AND WALTER C. WEIGNER (*Brain*, Volume LXI, Part 3, 1938) preface their detailed case report of Pick's disease with a review of the literature relating to this condition. The case is that of a married woman, fifty-six years of age, admitted to hospital because of personality changes and increasing restlessness. A diagnosis of Pick's disease was made, and this was confirmed four years later by *post mortem* examination, which revealed characteristic circumscribed areas of atrophy in frontal, temporal and insular areas. The finding of "Pick's cells" containing argentophile bodies is in sharp contrast to the senile plaques and Alzheimer's fibrillary degeneration found in other varieties of senile dementia. The authors state that the encephalogram is of diagnostic value. The memory defect in Pick's disease is different from that in the other dementias. The authors believe this to be a salient feature in the establishment of a differential diagnosis. In Pick's disease the memory itself is not so much disturbed as the ability to use it in the formation of new ideational material.

Tumours of the Thalamus.

G. E. SMYTH AND KARL STERN (*Brain*, Volume LXI, Part 4, 1938) have studied six patients presenting tumour of the thalamus—five gliomata and one sarcoma—to elucidate certain problems arising in the noted discrepancy between the symptomatology of thalamic tumours and the classic thalamic syndrome. Thalamic gliomata invade the brain in a lateral

direction and are characterized by the early onset of mental symptoms, rapid deterioration and early conjugate ocular palsies. Objective sensory disturbances, if not absent from the clinical picture, obtrude only in the late stages. Cases of thalamic neoplasm in which mental changes of a deteriorative type and iridoplegia are present may resemble general paralysis. The authors grouped their cases according to the site of the primary thalamic involvement and discovered that the clinical picture depended upon whether the medial or lateral regions of the thalamus were the first to become involved. The six case histories are supplemented with detailed clinical, histological and autopsy findings.

The Spinal Fluid in Active and in Inactive Multiple Sclerosis.

STANLEY M. DILLENBERG (*Bulletin of the Neurological Institute of New York*, September, 1938) has investigated the spinal fluid findings in 226 cases of multiple sclerosis. He draws attention to the fact that in a wealth of literature which surrounds this disease, Merritt alone has drawn attention to the changes in the spinal fluid in the stationary and progressive forms of multiple sclerosis. While there is no change in the cerebrospinal fluid which may be regarded as pathognomonic of multiple sclerosis, analysis of the fluid in many instances shows that in active cases there are greater degrees of abnormality than in stationary cases. Dillenberg found the sugar and chloride content to be within normal limits irrespective of the state of the disease. The number of cells was diminished in the inactive phases of the illness, 2.91 cells per cubic millimetre being the average in inactive and 6.7 cells per cubic millimetre in active cases. Globulin tests gave negative results in 58% of the active and in 78% of the inactive cases. Protein determinations revealed an average content of 44.24 milligrammes in active and 34.97 milligrammes in inactive cases. Gold curves proved difficult to judge; but all the strongly positive curves fell into the active disease group.

Granulomatous Encephalomyelitis due to a Protozoan.

ARNER WOLF AND DAVID COWEN (*Bulletin of the Neurological Institute of New York*, December, 1938) give a complete description of a case of granulomatous encephalomyelitis due to a protozoan. It is a disease of infants, and the protozoan is thought to be toxoplasma or encephalitozoon. Four other cases from the literature are cited and reviewed, and the identity of the causative micro-organism is discussed from the morphological viewpoint. The case reported is that of an infant admitted to hospital at the age of twenty-four days, suffering from fever, irritability and convulsions. The infant died

five days afterwards. Examination revealed an area of chorioretinitis in each fundus. The cerebro-spinal fluid was xanthochromic, with increased protein and globulin, and pronounced lymphocytosis was present. The fluid was sterile and failed to react to the Wassermann test. An extensive pathological report of the *post mortem* examination is given. This revealed widely disseminated encephalomyelitis; parts of the cortex were marked by intense inflammation and necrosis. Miliary granulomata were scattered throughout the central nervous system, and a protozoan parasite was found in these lesions. To the authors it seemed likely that the disease had its inception during intrauterine life.

Nocturnal Epilepsy in Cases of Brain Tumour.

JOHN D. SPILLANE (*Bulletin of the Neurological Institute of New York*, December, 1938) has studied the incidence of epilepsy occurring as a symptom of brain tumour in 507 proven cases. In this number only cases of cerebral and cerebellar tumours were included, as epilepsy is considered to occur very rarely as a result of pituitary tumours. Convulsions occurred in 201, or 44%, of cerebral cases; it was not found in the cerebellar cases. One or more nocturnal seizures were recorded in 53 cases, or 25%. In 69% of these 53 cases the nocturnal convulsion was actually the first symptom. The author points out an interesting fact, that not only was the nocturnal seizure the first symptom, but in 62% of these cases it was the only nocturnal seizure, the remaining convulsions occurring during the daytime. He notes also that diurnal seizures are thirty times more common than nocturnal seizures when such are the symptoms of cerebral tumours. In cases of idiopathic epilepsy, on the other hand, diurnal seizures are only approximately twice as frequent as the nocturnal convulsions. In the majority of patients presenting nocturnal epilepsy as a first symptom of cerebral tumour the growth was found to be in the frontal cortex.

Thrombophlebitis Occurring in Patients Receiving Barbiturates.

FROM a series of 150 patients who received barbiturates during the course of prolonged narcosis H. A. Palmer (*The Journal of Mental Science*, March, 1939) reports four who developed thrombophlebitis. All were males, and three out of the four were over fifty years of age. All recovered. The author, who regards the development of thrombophlebitis as one of the natural hazards of treatment, suggests the routine administration of small doses of potassium citrate during the narcosis and massage to the lower limbs as prophylactic measures. The condition responds to rest and the application of heat combined with belladonna.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Warrnambool and District Base Hospital on May 6, 1939, DR. F. L. DAVIES, the President, in the chair. Part of the meeting took the form of a number of clinical demonstrations by members of the honorary staff of the hospital.

Preeclamptic Toxæmia.

DR. IRVING BUZZARD read a paper entitled "Preeclamptic Toxæmia" (see page 55).

PROFESSOR MARSHALL ALLAN, in opening the discussion, congratulated Dr. Buzzard on his excellent survey of the cardinal points in the diagnosis and treatment of preeclamptic toxæmia. He said that such a paper was of the greatest value, because the toxæmic syndrome was closely allied to maternal mortality and morbidity, and to a greater extent to the mortality and morbidity of the infant. In surveying recent literature as to the exciting factor, Professor Allan discussed the part played by the absorption of guanidine, histamine and tyramine from placental infarction; but he said that it was difficult to adduce any conclusive proof. Excessive endocrine secretions had often been blamed for the derangement of water metabolism and for capillary spasm in vital organs. He reviewed the claim of Anselmino and Hoffmann to have isolated an antidiuretic hormone from the posterior pituitary, and said that their claims had been partly supported by research carried out by Dr. Krieger at the Women's Hospital. He stressed the need for an adequate supply of calcium during pregnancy, and added that calcium was not utilized nor retained in the body unless vitamin D was also given. Calcium was best administered by intramuscular injection. The work of Siddall on the effect of vitamin B₁ deficiency was explained in detail. It had been confirmed by Japanese observers, and De Lee was trying brewer's yeast to increase the vitamin B₁ content of his patients' diet. Professor Allan then discussed the statement of De Snoo that a salt-free diet was essential to prevent oedema, and also the possible effects of geographic distribution and climate. Despite the numerous theories put forward, the real cause of the toxæmia was still unknown.

Referring to diagnosis, Professor Allan explained two recent tests. The first, the cold pressor test, was one of vasomotor lability, and depended on the rise in systolic blood pressure that occurred when the arm was plunged into water at a temperature of 1° to 2° C. Any increase above 30 millimetres of mercury was considered abnormal. The test gave no uniform results in preeclampsia, but was most useful in the presence of a family history of hypertension or in cases in which it might be expected to develop in a subsequent pregnancy. The second test involved the estimation of the blood pressure after the injection of one to two minims of pituitary extract. This caused a decrease in the volume of urine secreted and a rise in the systolic blood pressure. The average increase in normal cases was 11 millimetres of mercury, as compared with 7 millimetres in hypertension and 51 in preeclampsia.

Discussing treatment, Professor Allan said that it should be as radical as that of eclampsia was conservative. All patients with a systolic blood pressure of 150 millimetres of mercury should be admitted to hospital, where sedatives and dietary restrictions should be instituted and elimination carried out thoroughly. The general tendency was to terminate the pregnancy within a short time if the patient's condition failed to improve or if an increase in the symptoms occurred. Regarding the method of termination, Professor Allan pointed out that nerve muscle irritability was lowered in toxæmia; hence the importance of remembering this fact when any particular method was being decided upon. He preferred tubal induction to

rupture of the membranes in most cases, especially with *primipara*. Finally, Professor Allan stressed the importance of the immediate care of the infant after birth, because it was generally premature and less vigorous than usual.

PROFESSOR P. MACCALLUM congratulated Dr. Buzzard on his comprehensive review. He referred first to the importance of mutual interactions of kidney disease and eclamptic and preeclamptic conditions. Though clearly the clinical condition indicated pathological states, primary or secondary, in other parts of the body (brain, blood, liver or endocrine glands) the combination of albuminuria, hypertension, oedema and convulsions inevitably directed attention to the kidney. Renal changes were no longer regarded as primarily responsible for the condition, but were in any case far from negligible, not only as factors in the development of the syndrome, but as lesions liable to aggravation by it. Even though urea estimation, dye excretion and other tests indicated no simple fixed relation to the severity of the condition, the estimation of kidney function was on both counts of profound significance to the patient. Hence improved understanding of biochemical tests and simplification of their interpretation for clinical use were desirable goals. Professor MacCallum directed attention to the work of Dr. Krieger, who had examined the significance of urinary volume in urea concentration tests under standard conditions, demonstrated their value and defined the conditions (for example, a small urea percentage in a large volume of urine) in which alone uncertainty might remain. He also circulated copies of and described the use of a simple nomographic chart devised by Dr. M. C. Davis, with which, from the data of a standard urea test (for example, urea concentration, blood urea content and minute volume) the efficiency of the kidney could be read off in terms of blood urea clearance as a percentage of the normal value. More precision was thus made available to the practitioner in his estimate of the condition and of the progress of kidney lesions and function in preeclamptic and eclamptic cases.

DR. IVON HAYES said that with assistance he had examined 3,500 records of confinements at the Women's Hospital, Melbourne, for the purpose of glean information about eclampsia and preeclampsia. The examples of transient albuminuria with systolic blood pressure between 140 and 170 millimetres of mercury had not been included in his summary as instances of preeclamptic toxæmia; the criteria indicative of eclampsia were the occurrence of generalized oedema, albuminuria and raised blood pressure associated with headache, epigastric pain and ocular symptoms. He had formed the opinion that renal function tests were not helpful in the diagnosis of preeclampsia. The incidence of preeclamptic toxæmia in the cases studied was one in fifty-seven of the patients who were regarded as belonging to the Women's Hospital and who had for the most part been under antenatal supervision there; but the incidence was one in thirteen among the "emergency" patients sent to the hospital for treatment and delivery who had not had that antenatal treatment. When all the cases were included the incidence was one in thirty-eight, which was approximately in agreement with the figure of 3% arrived at by Dr. Buzzard in his series of 1,197 patients. Two mothers and 27 children had died in the preeclamptic group at the Women's Hospital; but it was noteworthy that only ten of the children who had died had passed 36 weeks of intrauterine life. Of the 98 preeclamptic women, 54 were *primipara*; 66% of whom were between the ages of fifteen and twenty-five years; of 44 *multipara*, 60% were between thirty-one and forty years of age, and one-third of them had a previous history of renal disease. Dr. Hayes remarked that the occurrence of renal toxæmia always predisposed to further toxæmia in later pregnancies.

Discussing the relative methods of artificial rupture of the membranes and introduction of a tube into the rectum for the induction of labour when the patients did not promptly "deliver themselves", Dr. Hayes stated that he was biased towards artificial rupture. In the 1938 series artificial rupture had been used in eleven cases without

any deaths; and tubes had been inserted into the rectum in 21 cases, with two maternal deaths from sepsis—a 10% mortality rate. Over the past six years in preeclampsia artificial rupture of the membranes had been used in three cases without any deaths or much trouble, while the introduction of tubes into the rectum had been used in 216 instances with two deaths from toxæmia and five from sepsis; and in two other cases Cesarean operations had been performed after failure of rectal induction. Dr. Hayes said that his objections to the introduction of tubes into the rectum were that the procedure necessitated the introduction of a foreign body, the risk of separation or infection of the placenta or of prevention of the descent of the presenting part. The foreign body introduced a source of sepsis, or might cause accidental hæmorrhage; if the tube was introduced and allowed to hang down it prevented the normal stimulation of the cervix, and if it was pushed right inside it was difficult to know what should be done if there was a delay in termination of labour. There was not the same worry when the membranes were ruptured, as the method was more natural and there was less possibility of infection; there was also a quicker response. Dr. Hayes supported the last fact by stating that in the 1938 series the average delay after the rectal method of induction of labour was thirty-six hours, whereas the corresponding length of time after artificial rupture of the membranes was only twenty-three hours. The shorter interval was a definite advantage when it was recognized that the prolongation of the toxæmic state prejudiced the complete recovery of the kidneys. The general treatment of the condition was on accepted lines, with emphasis on early induction. The dangers of preeclampsia were the possible death of the child and risks to the mother of eclampsia, cerebral hæmorrhage, pulmonary oedema, infections, sepsis and permanent damage. Within two weeks Dr. Hayes had encountered five cases of preeclampsia. In the procedure of artificial rupture the membranes should be stripped up and some of the *liquor amnii* let out. Dr. Hayes considered that treatment in hospital for fourteen days, as advocated by Dr. Buzzard, was far too long; he would rather place the limit at ninety-six hours. After the patient had been admitted to hospital she should be purged and given water, glucose and chewing gum, and be allowed to smoke cigarettes. If she became worse under that treatment he carried out induction within four days; he was satisfied that if the patient's condition did not improve within four days it would be detrimental to wait fourteen, if only because of the added risk of further damage to the kidneys. If within four days material improvement was manifested, the diet could be progressively brought to normal. It was recognized that it was not the intensity of the toxæmia but the time factor that left permanent kidney damage. The mother had to be saved from morbidity, irrespective of the fate of the fetus.

DR. JOHN GREEN said that the subject had always interested him, and briefly reviewed the history. He said that in 1797 Cruickshank had written about the association between albuminuria and oedema, and in 1827 Bright, of Guy's Hospital, had linked those signs with kidney damage. It was at Guy's Hospital also that Lever had discovered that eclamptic women had albuminuria, and in 1867 Braxton Hicks had announced the new departure that pregnancy itself could be a cause of chronic nephritis. Braxton Hicks had thought that he would look up records of the state of the urine in pregnant women, and had been able to find the results of only fifty tests; so he had tested another fifty specimens and from that investigation had drawn his conclusions. Dr. Green added that the occurrence of raised blood pressure was recognized long before the sphygmomanometer had been invented, and it had interested him to note that Dr. Buzzard had appreciated the value and importance of blood pressure readings. At that stage Dr. Green passed over to the chairman and to Dr. Buzzard a monograph on albumin in the urine that had been published in 1839; he commented on the profit and interest he had gained by its perusal.

Dr. Green went on to say that in eclampsia the management of the patient had to be very personal and very intense. At the Women's Hospital it was regrettable that so many of their own patients became toxæmic before confinement; but it was very difficult to influence effectively the management of the patient between visits to the antenatal clinic, and indeed some of the patients began to have fits while actually in the hospital awaiting delivery. There was a swing towards the suggestion of vitamin deficiency as a causative factor, and Dr. Green believed that the diet should have quite an appreciable energy value; he was entirely of the opinion that the treatment adopted influenced the course of events, though more thought was necessary concerning the appropriate handling of the situation after induction of labour. With reference to the controversy between the relative merits of artificial rupture of the membranes and tubal induction, Dr. Green said that he was inclined to favour tubal induction, because it provided a way of escape. If no labour eventuated within forty-eight hours after the introduction of the tube it was difficult to know what to do. It was his practice to take the tube out on the third day, as the risk if it was left in was greater than the risk that the patient might have fits, and some time later the baby might be delivered naturally. Dr. Green advised against rupture of the membranes, because he felt that he did not know what the patient was going to do, and if the procedure was not effective it might be the cause of considerable trouble to the mother.

Dr. Green expressed his diffidence about the administration of general anaesthetics to toxæmic pregnant women. He said that he introduced the tube into the rectum with the patient under the influence of morphine and hyoscine. Speaking of prognosis, he said that it had to be recognized that the kidneys had remarkable power of recovery after preeclamptic toxæmia, and that it was very gratifying to be able to assist the patient to prolong the pregnancy successfully for five or six weeks. The outlook for subsequent pregnancies was not necessarily bad, and the different sequences encountered were somewhat surprising. Though he realized that opinions differed on the matter, he was satisfied that it was not justifiable to forecast confidently that a patient who had primarily experienced severe toxæmia in pregnancy would have recurrent toxæmia during further pregnancies. Pregnancy in patients with chronic nephritis was more likely to be associated with exacerbations; but, speaking broadly, he believed that the condition was much less alarming than primary preeclamptic toxæmia.

DR. W. R. ANGUS said that in fifteen years of general practice he had encountered only two instances of real eclampsia, one of which was, in his opinion, precipitated by a dietetic indiscretion. He had been impressed with the degree of liver inefficiency associated with preeclamptic toxæmia, and regarded general anaesthesia as contraindicated until liver efficiency was reestablished. Investigations of hepatic adequacy rather than of renal efficiency seemed to him to be worth while. The water concentration test of renal efficiency was a useful clinical test, and as reliable as the other tests to which previous speakers had referred. From the preventive aspect Dr. Angus thought that all were agreed on the fundamental importance of careful attention to the diet in pregnancy, and under the heading of treatment he would include mild non-surgical biliary drainage in selected cases. The performance of Cesarean section in the presence of eclampsia was a very hazardous undertaking that should be avoided if possible. Dr. Angus concluded by emphasizing the importance of the liver as an organ fundamentally affected in eclampsia.

DR. Z. SCHWARTZ drew attention to the serious consequences of neglect of the ocular lesions in retinitis of pregnancy, which might occur with or without papilloedema. Papilloedema might occur alone; but the presence of albuminuric retinitis was evidence of gross damage. Papilloedema should not be allowed to continue for long without appropriate treatment.

DR. A. N. HILL spoke of the latent period between the time of induction and the onset of labour. He did not

like the interval to be prolonged beyond five days, and he was inclined towards the views expressed by Dr. Hayes. The problem for him was not so much the recognition of the fact that *primiparae* were likely to have healthier kidneys than older women, but that kidney damage would prejudice the future even of young *primiparae*.

Professor Marshall Allan spoke again to inform the meeting that the question of hepatic affection in pre-eclampsia and eclampsia had been the subject of investigation at the Women's Hospital some ten years earlier, and that they had had very little assistance from the results of the biochemical tests. From observance of the clinical facts it was apparent, however, that the liver was one of the principal organs affected.

Dr. Irving Buzzard thanked those present for the manner in which his paper had been received.

Relaxation of the Symphysis Pubis in Pregnancy.

DR. IRVING BUZZARD demonstrated from a series of skiagrams the appearances of relaxation of the *symphysis pubis* in pregnancy. He explained that the skiagrams were taken in pairs, the patient standing on either leg on a block of wood, with the other leg swinging free; by comparison of the pair of films an idea could be obtained of the degree of mobility and separation at the symphysis. Dr. Buzzard pointed out that the condition might be antenatal or post-natal, and classified the main symptoms and signs. He remarked that the degree of separation or movement did not necessarily run parallel with the severity of the signs or symptoms, and that the pain and inconvenience, though continually tending to diminish, could persist for more than a year. He added that one woman who had developed the condition with the birth of her first child suffered from it antenatally during her second pregnancy.

Dr. Buzzard said that the main symptoms were: (i) aching pain in the *symphysis pubis*; (ii) pain in both pubic rami, shooting down the inner sides of the thighs; (iii) the sensation of being torn apart; (iv) inability to turn over in bed without great discomfort; (v) much more severe pain on movements such as getting in or out of bed or attempting to stand after sitting down. The main signs to which he referred were: (i) waddling gait; (ii) tenderness on palpation over the *symphysis pubis* and down one or both of the pubic rami; (iii) a sulcus, which might be felt between the two pubic bones; (iv) pain or movement, elicited by means of a "push and pull" test; and (v) pressure of the iliac crests outwards causing great pain over the symphysis.

PROFESSOR MARSHALL ALLAN said that the skiagrams shown by Dr. Buzzard were illustrative of extreme instances of the separation of the *symphysis pubis*, which occurred physiologically during pregnancy. He remarked that the oestrogenic hormone of the ovary might cause some softening of the pubis. In a series of seventy-eight cases in which he had analysed the radiographic appearances late in pregnancy, a separation of approximately six millimetres occurred in nearly half of them; but in most instances union had followed soon after the termination of the pregnancy. The separation did not seem to bear any relationship to the size of the pelvis, the size of the fetus or the type of labour. Dr. Buzzard had testified that the condition could be troublesome; but the majority of patients seemed to recover quickly. Some of the pain and aching and difficulty in walking during pregnancy might be due to the relaxation. In the guinea-pig there was a very wide separation. Professor Marshall Allan said that a corpus luteal hormone might be indicated in treatment, or perhaps some enterprising surgeon might design an operation for putting staples in to hold the pubic bones together; but there was nothing definite in the obstetric literature.

DR. BRYAN KEON-COHEN observed that there was quite a diminution in clarity of the outline of the pubic bones; this had made him wonder whether there had been any preexistent osteochondritis. He also stated that he had

seen somewhat similar appearances in skiagrams of the pelvis of men injured at heavy work; but in those cases the effects had not been lasting. Dr. Keon-Cohen made the further suggestion that a small graft might be placed across the symphysis in selected cases, though all but exceptional patients would recover satisfactorily after prolonged recumbency.

DR. J. B. COLQUHOUN said that staples would not stay in position for more than two weeks, but that Krupp's stainless steel wires might prove satisfactory.

DR. W. G. CUSADEN thought that some osteochondritic change must take place, because when traction was exerted with obstetric forceps the pubes might crack or even come adrift.

Radiological Exhibits.

DR. J. F. PATRICK showed a series of skiagrams, all of which had been prepared at the Warrnambool Base Hospital during the preceding eighteen months. The following subjects were represented in the display of films: bone lesions in carcinoma of the prostate, in sarcomatous Hodgkin's disease and in leucemia; secondary carcinoma of the spine; *osteitis deformans* with sarcomatous change; *osteitis deformans* of a lumbar vertebra; cyst-like changes in carpal bones; ununited epiphysis of the inferior articular process of a lumbar vertebra; bilateral synostosis of the proximal ends of the radius and ulna; union of all epiphyses in the region of the elbow joint at the age of twelve years and eight months; fracture of the lateral tubercle of the talus; fracture of the anterior-superior border of the calcaneus; longitudinal fracture of the distal end of the humerus; *spina bifida occulta* of the seventh cervical and first thoracic vertebrae; *spondylitis deformans* (Marie-Strümpell); hydatid cyst of the lung; inferior accessory lobe of the right lung; abscess of the lung; two instances of diverticulosis of the colon; carcinoma of the cardiac end of the stomach and oesophagus; opaque and non-opaque gall-stones; gall-bladder with folding of fundus; diverticulum of the urinary bladder; chronic osteomyelitis of the femur; and chondromata of the bones of the hand.

DR. JOHN O'SULLIVAN congratulated Dr. Patrick on the excellent technical results he had obtained with equipment which would not be considered adequate by radiological specialists in the city. He considered that Dr. Patrick's work at the hospital was of such a high order of importance that his colleagues and the management of the hospital should encourage and support him if and when he asked for better equipment.

Gunshot Wound of the Shoulder.

DR. H. I. HOLMES showed a female patient, aged eighteen years, who had been admitted under his care to the Warrnambool Base Hospital on January 10, 1939, in a grave condition as a result of an accidental gunshot wound of the right shoulder. The gun had been fired at a distance of not more than a foot or two. There was doubt as to whether the pulse could be felt at the wrist, and the probability of amputation was considered. After the preparation of skiagrams the wound was investigated surgically; the wads of the cartridge and several shot were removed in addition to a piece of detached bone. After some attempts at repair the wound edges were brought partly together with silkworm gut sutures. The pulse was quite perceptible next day and the arm was kept on an angular splint in partial abduction for several weeks. From the skiagrams shown and from examination of the patient it could be seen that the bone had been shattered and that large numbers of shot were present in the arm, shoulder and chest, but that the fractures had united. Dr. Holmes showed that there was good recovery of the forearm movements, though those at the shoulder were limited. He pointed out the escape from damage to the main vessels and nerves in the axilla, and the satisfactory circulation and absence of definite nerve-paralysis. He asked for expressions of opinion as to

whether primary closure should have been attempted, whether he should have made a better realignment of the fragments of bone, and whether anything could have been done to gain greater function. He also sought advice as to the best procedure to adopt with the cavity which remained at the time of the meeting.

DR. BRYAN KEON-COHEN said that Dr. Holmes had obtained a satisfactorily useful limb. In his opinion such a wound should be left open, with free drainage, and small foreign bodies overlooked or out of reach at operation would be discharged. He thought that Dr. Holmes's patient would continue to have a sinus track for years, which would be liable to break down even after healing had taken place.

DR. S. C. FITZPATRICK said that he had had two patients with somewhat similar gunshot wounds of the axilla. He thought that the accident arose from the bad habit of sitting on the haunches with a loaded gun resting against the shoulder; when the person so supporting the gun sprang to his feet the trigger would move and the gun would be discharged into the axilla. In each of the cases to which he had referred infection had been controlled by the instillation of eusol or felsol solution. Progress had been satisfactory because no large vessel or nerve had been involved; that could be regarded only as a matter of sheer luck.

DR. C. H. OSBORN asked Dr. Holmes whether he would consider giving the arm another period of abduction. The patient did not appear to have septic arthritis of the shoulder joint, and further abduction might be beneficial until the inevitable sequestrectomy was performed; the scarring area would thus be kept stretched.

Dr. Holmes, in reply, said that the frame had been in the position of half abduction and not full abduction because of the fear of gangrene. He added that a small piece of clothing fabric had come away from the wound in the early stages.

Parathyroid Tumour and Fibrocystic Disease.

Dr. Holmes also showed a male patient, aged twenty-two years, who had come under his care on June 18, 1938; he had sustained a fracture of the upper portion of the shaft of the humerus following a fall onto the hand. From the skiagrams it had been apparent that the patient had fibrocystic disease of the osseous system; fibrocystic changes were evident in the humerus on each side, in the femora, scapulae and to a slight degree in clavicular and acromial regions. The erythrocytes numbered 3,700,000 and the leucocytes 25,000 per cubic millimetre, and the haemoglobin value was estimated at 70%. The Casati intradermal test elicited no reaction. Dr. Holmes stated that previously, on April 20, 1936, the patient had been seen at the hospital because of vague ill health; he had then been an in-patient for eleven days, suffering from pain in the left upper portion of the abdomen.

Dr. Holmes said that the patient had come under the care of Dr. S. V. Sewell, and that a parathyroid tumour had been removed from behind the right lobe of the thyroid gland by Dr. Henry Searby. At the time of the meeting the erythrocytes numbered 4,030,000 and the leucocytes 5,750 per cubic millimetre, and the haemoglobin value was 75%. The blood calcium content was 17.6 milligrammes per hundred cubic centimetres of blood when Dr. Sewell first saw the patient, and forty-eight hours after the removal of the tumour it had dropped to 10.2 milligrammes and had remained between nine and ten milligrammes ever since.

DR. S. V. SEWELL showed the preserved tumour, a prepared microscopic section of it, and a series of skiagrams prepared at the Royal Melbourne Hospital. He gave an interesting account of the relationship between parathyroid tumours and fibrocystic disease of the osseous system, and remarked that the present patient was the second who had been treated at the Royal Melbourne Hospital by removal of the tumour.

(To be continued.)

NOTICE.

THE Section of Medicine of the New South Wales Branch of the British Medical Association will hold its annual clinical evening on Thursday, July 13, 1939, in the Robert H. Todd Assembly Hall, 135, Macquarie Street, Sydney, at 8.15 o'clock p.m.

Cases of hyperchromic anaemia following gastrectomy, of spastic speech, of pellagra, of dwarfism with optic atrophy, of exophthalmic ophthalmoplegia in hypothyroidism, and of osteitis fibrosa disseminata will be presented respectively by Dr. Innes Brodziak, Dr. A. J. Collins, Dr. K. B. Noad, Dr. A. J. Hood Stobo, Dr. E. H. Stokes and Dr. B. T. Shallard. The discussion in these several instances will be opened by Dr. C. G. McDonald, Dr. A. W. Morrow, Sir Charles Blackburn, Dr. A. W. Holmes & Court, Dr. Cedric Cohen, and Dr. Lorimer Dods and Dr. H. R. Sear. Dr. Douglas Anderson will discuss and give a demonstration of tomograms, and Dr. G. Bruce White will open the discussion on them.

The members of the section invite all members of the Branch to be present and to take part in the discussion.

The Royal Australasian College of Physicians.

EXAMINATION FOR MEMBERSHIP.

THE following candidates were successful at the examination for membership held in Melbourne in March, 1939, and have been admitted as members of the college: Dr. C. W. Adey, Dr. R. C. E. Brodie, Dr. K. B. Burwood, Dr. J. L. Frew, Dr. A. W. M. Hutson, Dr. J. E. Sewell, Dr. A. J. M. Sinclair, Dr. W. McL. Smithers, Dr. A. G. H. Springthorpe and Dr. E. R. Trethewie, of Victoria; Dr. W. E. L. H. Crowther, of Tasmania; Dr. Addie Walker, of New South Wales; and Dr. R. F. West, of South Australia.

The following were also successful at the membership examination held in Dunedin, New Zealand, in May: Dr. J. D. Cottrell and Dr. A. McIlroy, of Dunedin; Dr. E. S. Stubbs, of Oamaru; and Dr. R. F. Wilson, of Auckland.

Forthcoming Examination, August-September, 1939.

Intending candidates for the forthcoming examination for membership of the Royal Australasian College of Physicians are reminded that applications for this examination should be in the hands of the honorary secretary not later than July 22.

The written paper will be taken on Saturday, August 19, and the corresponding clinical examination will be conducted in Sydney on Wednesday and Thursday, September 6 and 7, 1939. Application forms are obtainable from the office of the college, 135, Macquarie Street, Sydney.

Post-Graduate Work.

WEEK-END COURSE IN MEDICINE AT SYDNEY.

THE next week-end course in medicine at the Prince Henry Hospital, arranged by the New South Wales Post-Graduate Committee in Medicine, will be held on September 2 and 3, 1939, and not on September 9 and 10, as originally announced. A programme of the course will be published shortly.

POST-GRADUATE COURSES IN BERLIN.

THE Berliner Akademie für Ärztliche Fortbildung is holding the following medical post-graduate courses in autumn, 1939:

1. Post-graduate course in orthopaedics (from September 11 to 16). Fee: 50 RM.
2. Courses on tuberculosis (from September 21 to 27). Fee: 50 RM, 25 RM respectively.
3. Post-graduate course in heart and vascular diseases (from October 2 to 7). Fee: 50 RM.
4. Influence of weather, seasons and similar factors on health and ill health of men (from October 9 to 14). Fee: 50 RM.
5. Skin and venereal diseases, including cosmetics (from October 9 to 14). Fee: 75 RM.
6. The importance of Röntgenology in internal medicine (from October 16 to 21). Fee: 60 RM.
7. Obstetrical and gynaecological post-graduate week (from October 23 to 28). Fee: 50 RM.
8. Post-graduate course in diseases of the ear, nose and throat (September-October). Fee for the whole course: 150 RM; for the theoretical part of the course: 100 RM.
9. Surgery of intrathoracic diseases, with special regard to pulmonary tuberculosis (from October 23 to 27). Fee: 80 RM.
10. Preliminary training course in homeopathy (from October 9 to 28). Fee: 60 RM.
11. Special courses in all branches of medicine, with practical work at the bedside and in the laboratory, to be held every month. For these courses participants are requested to communicate their wishes in order to find a complete programme on their arrival.

Courses 1 to 10 will be held in German, and the special courses also in foreign languages.

For programmes and further information apply to the Geschäftsstelle der Berliner Akademie für Ärztliche Fortbildung, Berlin, NW7, Robert Koch-Platz 7 (Kaiserin Friedrich-Haus).

The German State Railways grant a reduction of 60% to foreign doctors and to German doctors residing abroad; foreign doctors can reduce the cost of the stay considerably by utilizing the so-called "registered marks"; it is advisable to arrange matters with the local bank before starting.

Research.

THE INTERNATIONAL STANDARD FOR THE GONADOTROPHIC SUBSTANCE OF HUMAN URINE OF PREGNANCY: CHORIONIC GONADOTROPHIN.

THE Director-General of Health, Commonwealth Department of Health, has forwarded for publication the following statement.

A small quantity of the international standard for the gonadotrophic substance of human urine of pregnancy, chorionic gonadotrophin, has recently been received from the Director of the Department of Biological Standards, London, at the Commonwealth Serum Laboratories, which laboratories act as the distributing centre for Australia for this and other international standards.

Institutions or research workers requiring samples of this standard for reference purposes should make application to the Director, Commonwealth Serum Laboratories, Parkville, N.2, Melbourne.

When the standard is distributed on receipt of such application, a copy of the official memorandum from the League of Nations Health Organization, dealing with the standard, will be forwarded to the applicant.

KING GEORGE V AND QUEEN MARY MATERNAL AND INFANT WELFARE FOUNDATION.

To mark the jubilee of King George V and Queen Mary funds were provided by public subscription and by grants from the Commonwealth and State Governments, the fund being known as the King George V and Queen Mary Maternal and Infant Welfare Fund.

Legislation passed in 1937 established a foundation in which the funds have been vested. The income of the fund will be applied by the foundation to grants in aid of the work of investigation and research into the causes and treatment of maternal and neonatal morbidity and mortality and the encouragement of research and post-graduate teaching in relation to maternal and neonatal welfare.

Applications are being invited by the foundation for grants in aid of the work referred to. Forms of application and terms and conditions under which grants will be made are obtainable on request at the office of the Director-General of Public Health, New South Wales.

Correspondence.

ENDEMIC TYPHUS IN NEW GUINEA.

SIR: In reference to the article by Dr. Gunther and Dr. Schroeder in the journal of May 6 last, describing two cases of bush typhus at Wewak, I would like to add a matter of interest.

The previous cases referred to were all diagnosed by the Well-Felix reaction, giving the same results as those now described (OXK—1/1,280). None of them, however, were severe, and one so mild that I only noticed the rash in casually meeting the patient. It is evident that there is great clinical variation in this disease, and in the mild case, though the serum reaction is positive, the eschar seems to be missing.

I have been struck in the past with the curious resemblance these mild cases bear to cases of *pityriasis rosea* that I saw in Sydney hospitals, and I would suggest as a possible interesting line of research the taking of Well-Felix reactions in some of these.

The more one sees and hears of typhus, the more there seems to be awaiting discovery.

The suspensions I used were supplied to me by the courtesy of Professor Harvey Sutton and Dr. Sawers, of the School of Public Health and Tropical Medicine, Sydney.

Yours, etc.,

C. MERVYN DELAND,

M.B., B.S., D.P.H., D.T.M.

Manus,
New Guinea,
June 3, 1939.

"THE LISTERIAN IDEA IN THE YEAR 1939."

SIR: This is the title of Professor René Leriche's Lister Memorial Lecture given before the Royal College of Surgeons of England on the anniversary of Lister's birth this year. The editorial comment on this lecture (*The British Medical Journal*, April 15, 1939), that it "is before everything else a protest against conservatism", is true in more ways than one, unfortunately. The leading article points out that Lister himself had to contend and did contend most valiantly against self-complacency and bigotry in his own day, and in spite of Professor Leriche's vigorous advocacy someone has still got to do it. The idea that Lister aimed at destroying germs in a wound was fixed from the first, and the Lister Memorial lecturer perpetuates this monstrous error not only in word but in deed. It is quite meritorious to make the trial of

killing infection wherever it may happen to occur, but to say that this proceeding is a fundamental principle in the antiseptic method is utterly wrong and misleading to a harmful degree, because it obscures and turns attention away from what is the essence and only true idea of Listerism. This is nothing more or less than the provision of an outlet or means of evacuation for the wastage of contending forces with every precaution against interference from without. By this effective blockade (antiseptic) the invaders cannot possibly be reinforced while the besieged have no obstacle in the way of calling all the aid the full and plentiful resources of the body have at call. That these are powerful and could be relied upon is a fact that Lister was the first to proclaim.

Yours, etc.,

Wickham House,
Wickham Terrace,
Brisbane.
June 6, 1939.

A. C. F. HALFORD.

FOOD POISONING.

SIR: During the late autumn of this year a number of cases of poisoning, due to the ingestion of cooked mushrooms, have occurred in this district.

The symptoms came on rapidly after ingestion, and resembled those which occurred in two cases of duboisine poisoning (one of which was fatal) I treated some years ago. Mental confusion, unsteadiness of the limbs, dry mouth, flushed face, dilated pupils, visual hallucinations, and in a few cases noisy delirium. The importance of this observation is that most books on toxicology advise atropine hypodermically in the treatment of mushroom poisoning; this would only accentuate these symptoms.

The mushrooms are almost certainly *Psalliota arvensis*, var. *iodoformis*, and have a distinct iodoform odour, both in the field and during cooking.

The Government analyst was unable to find alkaloid in the cooked specimens submitted to him.

Yours, etc.,

GEORGE H. HEWITT, M.B., Ch.M.

Park Street,
Bellingen,
New South Wales.
June 16, 1939.

CROHN'S DISEASE.

SIR: The report of two cases of Crohn's disease by Dr. J. C. Bell Allen, and the apparent rarity of the disease in Australia, prompts me to refer to three cases in my own practice.

Case 1.—J.R., aged fifty years, a station hand, was first seen by me on January 20, 1938. He had had severe intermittent cramps in the mid and lower abdomen, accompanied by vomiting for the previous eight hours. The bowels had acted twice during this period, the motion being described as normal in consistency. The lower abdomen was markedly tender, more so to the left side, and there was clinical evidence of fluid in the abdominal cavity. Temperature was 97° F. and pulse 108 and of poor volume. At operation through a paramedian incision in the lower abdomen the peritoneal cavity was found to contain free blood-stained fluid in considerable amount. A portion of the terminal ileum was acutely congested, bright red, thickened and oedematous, being about fifteen inches long, with distal end about two feet from the ileocaecal junction. The affected portion of bowel was fairly sharply demarcated from adjacent healthy bowel. Removal of fluid and appendicectomy were carried out and a drain left in the pelvis for forty-eight hours. Post-operative history was uneventful, except for the recurrence on several occasions of what the patient described as like the original pains, but not very severe. He has now been perfectly well for sixteen months.

Case 2.—In the case of E.C., aged thirty, a shearer, operation for acute appendicitis (of twenty-four hours' duration) was performed on June 7, 1938. The abdominal cavity contained straw-coloured fluid, the appendix appeared to be quite healthy, and about fifteen inches of lower ileum showed the typical condition described in the previous case. Appendicectomy and closure of the abdomen without drainage were followed by uneventful convalescence, and there has been no recurrence of symptoms.

Case 3.—In the case of J.T.B., aged seventy, operation on October 27, 1938, was prompted by the sudden onset of acute abdominal pain, vomiting and rigidity. There had been increasing constipation and some loss of weight. The abdomen contained a considerable amount of blood-stained fluid, and a portion of lower ileum, about twelve inches in length, showed the characteristics already described in the previous cases. Convalescence was uneventful, and since the first two weeks there has been no recurrence of symptoms.

White cell and red cell counts gave no useful information in these three cases. The results of agglutination tests were negative, except that one case showed a mild positive result with *Bacillus dysenteriae*. The subsequent history of these cases, showing freedom from symptoms for periods of sixteen months, twelve months and seven months, supports Dr. Bell's suggestion that conservative treatment is justified. In my own cases operation proved to be diagnostic rather than therapeutic, as a preoperative diagnosis was not made in any of the three. The age of the third patient, seventy years, is well beyond the accepted age range of the disease.

Yours, etc.,

J. ANDREW ARRATTA, M.B.

Muttaborra,
Queensland,
June 21, 1939.

PROFESSOR OSBORNE'S PORTRAIT.

SIR: I should like through your columns to extend my warmest thanks to those old pupils and friends in the profession who thought of and made possible the presentation of my portrait to the university. No action of theirs could be more deeply appreciated by myself nor be so abiding a source of pride. Mr. Victor Hurley spoke on behalf of the donors at the ceremony last Wednesday in terms which I should like to imagine I deserved. My thanks are also due in large measure to the artist, Mr. McInnes, who was so patient with a sitter unaccustomed to sustained immobility.

Yours, etc.,

W. A. OSBORNE.

Lowestoft,
Warrandyte,
Victoria.
June 22, 1939.

Obituary.

MARGUERITE KETTLE.

News comes from England of the death of Dr. Marguerite Kettle, Assistant Editor of *The Lancet*. She was known to many Australian medical practitioners who visited England, and was recognized by them as a competent journalist and a talented and cultured woman. She impressed the visitor by her forceful personality, by her directness and by her insight. She studied medicine at Saint Mary's during the Great War, and here she worked under the late Edgar Hartley Kettle, who became known later on to Australians as the Director of the Department of Pathology of the British Postgraduate Medical School.

After she qualified in 1918 by taking the diplomas of membership of the Royal College of Surgeons of England and Licentiate of the Royal College of Physicians of England, she married Edgar Hartley Kettle. It was very soon after this that she joined the staff of *The Lancet* as a part-time officer. We are told in the warm-hearted tribute to her work in *The Lancet* of May 13, 1939, that "work on a child-welfare journal which had just then started gave her an almost fortuitous introduction to the editorial room of *The Lancet*, and this led to a half-time engagement". From the same source we learn that among her successes were the articles on "Modern Technique in Treatment" with which we are all familiar, and other series, including "Clinical Interpretation of Aids to Diagnosis"; she had charge of the interesting "Grains and Scruples", which are still appearing. The following short passage from this issue of *The Lancet* describes her mental attitude and her keenness in so delightful a way that it must be quoted:

To the office, as a nominally part-time worker, she came with an external point of view, based on the contacts of her immense acquaintance among practical and busy people—many of them pathologists—who liked facts rather than theories. She never for a moment believed that the truth is revealed to babes, and with a surprising orthodoxy she accepted the views of experts unquestioningly, so long as she believed them to be expert. She had little use for suggestive evidence and still less for suggestive hypotheses; though she could say so with great politeness. She was never impressed by mere novelty.

If as a realist she had a chastening effect on her collaborators she had an immensely stimulating effect on *THE LANCET*. More and more her function, as a part-timer having less routine to manage, was to prevent monotony and introduce new thought and new ideas. The ideas may not have been more frequent than other people's: the difference was that the moment one was seen it filled her mind. A casual remark in a letter from an aunt would strike her, and she would interrupt everyone's work for a morning while she discussed its implications. Three long (and unescapable) telephone conversations would follow; she would sit up half the night; and next day there would be a leader on her aunt's dilemma, or a scheme for a series of articles that would be useful to her aunt's doctor.

By the death of this gracious and gifted woman medical journalism in Great Britain, and in the Empire, has lost one of its most efficient workers. To her colleagues at 7, Adam Street, London, we offer our sympathy.

STEPHEN HAROLD COOKE.

Dr. W. L. POTTER, Melbourne, forwards the following appreciation of the late Dr. Stephen Harold Cooke.

Stephen Harold Cooke, who died in Melbourne on April 12, 1939, was the only child of the late John Cooke, a prominent practitioner of his day and for many years surgeon to the Alfred Hospital, Melbourne. He much resembled his father in sturdiness of character, modest unassuming ways, and entire absence of selfish ambition or self-seeking. He was a nephew of the late Dr. Charles Player, of Melbourne, bringing in medical interests on his mother's side.

Stephen Cooke was born at Prahran sixty years ago, and educated at Hallebury College and the Church of England Grammar School, Melbourne. In due time he proceeded to Melbourne University, where he completed the earlier years of the medical course; he then went to England and continued his course at the London Hospital, his father's *Alma Mater*, taking the diplomas M.R.C.S. (England), L.R.C.P. (London) in 1914. He volunteered for service on the outbreak of war, but was rejected because of ear trouble, and therefore continued his hospital work. In

1914-1915 he was resident at the London Hospital and assistant medical superintendent at the Chelsea Hospital for Women. Towards the end of 1915 he returned to Australia, having in the meantime married Daisy Revett, of Southampton.

Dr. Cooke showed no desire to follow surgery in the city, as his senior had done. He had a liking for general practice and country life, and was not deterred by the isolation and responsibility of practice in "one-man" districts, which class of work he followed in Victoria throughout his professional life. He commenced practice in 1916 in Myrtleford, where he remained eight years; then for eleven years at Nyah West, two years in Winchelsea, and about a year at Glenthompson. On account of ill health he forsook country practice, and early this year came to Melbourne, intending after twelve months' rest to resume practice under easier conditions in the city; but a serious development of the earlier condition set in suddenly, and in a few hours he had passed away.

Stephen Cooke married as his second wife, in 1922, Esther Hubbard, of Canterbury, Kent, England.

He identified himself with country life; he was interested in outdoor sports and fond of motoring, spending many vacations on long tours. For over twenty years he was an elder of the Presbyterian Church. He liked the quiet ways of the country and worthily filled the place he chose in the broad mosaic of medical service. He was companionable, a trusted friend, a courteous, kind and gentle attendant to those who came under his care.

Stephen Cooke leaves a widow, the mother of his one daughter, and two sons by his first marriage. The burial service was conducted by his old friend and school mate, Canon Crotty.

JOHN BINNY HAY.

We are indebted to Dr. W. Harlow Matheson for the following account of the career of the late Dr. John Binny Hay.

With the death of John Binny Hay at Mont Albert, Melbourne, on May 25, 1939, in his seventieth year, the medical profession has not only lost a sound and experienced physician, but a gallant gentleman, whose whole life has been marked by a gay indomitable courage, a whimsical dignity and an ethical outlook as unbending as the Hippocratic oath itself.

Born at Ceres, South Africa, in 1870, the son of George Charles Hay, M.D., of Edinburgh, he went to Edinburgh at an early age and was educated at the Edinburgh Academy and later the Edinburgh University, whence he graduated M.B., C.M. in 1895.

His adventurous spirit then led him back to South Africa, where, with a survey party in connexion with the overland Cape to Cairo telegraph, he penetrated as far as Bechuanaland. He then came to Australia for a short period, but on the outbreak of the Boer War offered his medical services first in London and then later in Capetown. Not being a regular military doctor, he was left marking time in the latter place till, his patience exhausted, he went in 1900 to the Gold Coast, West Africa, and was appointed assistant colonial surgeon with the British troops in the Ashanti campaign. During this grisly campaign he was several times mentioned in dispatches for bravery in action and was wounded in rescuing, "under circumstances of considerable peril", the body of a native officer. He was with the force that was besieged in Kumasi, and when, owing to shortage of water and provisions, it became necessary for the bulk of the force to fight its way out for relief, Hay was one of three white officers who volunteered to stay behind and attempt to guard the fort. The feat is a matter of history that thrilled the world at the time. His description of the cocktail he concocted from medical stores the night before their rescue, and when they expected not rescue but extermination, was a masterpiece of storytelling and of the pharmaceutical art.

For conspicuous bravery he was created C.M.G. in 1901, but had he been a regular military doctor the V.C. would have undoubtedly been his award.

For twenty-three years after his return to Australia Hay carried on a very busy and extensive general practice at Moonee Ponds, Melbourne; but the climate and privations of the Gold Coast had set their deteriorating mark upon his health and resistance, and at a comparatively early age he was forced to relinquish general practice and go into semi-retirement. For the past thirteen years he had resided at Mont Albert.

To those of us who were privileged to know him well, it was a matter of conjecture whether in a long courageous life his greatest courage of all was not shown in his latter years, when with quip and anecdote, and an unquenchable spirit, he fought his besetting demon, asthma, and did a measure of excellent work.

To Mrs. Hay and her three daughters the utmost sympathy of the medical profession will go. Those of us who knew and loved him have lost a very dear and charming friend.

ALAN HOBART STURDEE.

We regret to announce the death of Dr. Alan Hobart Sturdee, which occurred on June 19, 1939, at Sandringham, Victoria.

JAMES MORRIS ROE.

We regret to announce the death of Dr. James Morris Roe, which occurred on June 21, 1939, at Brisbane, Queensland.

THOMAS MURPHY.

We regret to announce the death of Dr. Thomas Murphy, which occurred on June 27, 1939, at St. Kilda, Victoria.

GEORGE HENRY SKINNER.

We regret to announce the death of Dr. George Henry Skinner, which occurred on June 27, 1939, at North Brighton, Victoria.

ALFRED QUIRK OGILVIE HARRISON.

We regret to announce the death of Dr. Alfred Quirk Ogilvie Harrison, which occurred on June 30, 1939, at Mudgee, New South Wales.

Proceedings of the Australian Medical Boards.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act, 1912 and 1915*, of New South Wales, as duly qualified medical practitioners:

Cass, Benjamin Phineas, M.B., B.S., 1925 (Univ. Melbourne), Prince Henry Hospital, Sydney.

Reid, William Lister, M.B., B.S., 1931 (Univ. Adelaide), 54, Cranbrook Road, Bellevue Hill.

Szanto, Geza, L.R.C.P., L.R.C.S. (Edinburgh), L.R.F.P.S. (Glasgow), 1939, c.o. Messrs. Garrett, Christie and Buckley, 14, Martin Place, Sydney.

Gooden, John O'Shaughnessy, M.B., B.S., 1939 (Univ. Melbourne), Base Hospital, Wagga Wagga.

Burt, Laurence Ian, M.B., B.S., 1939 (Univ. Sydney), General Hospital, Brisbane.

Bishopverder, Ernest, L.R.C.P., L.R.C.S. (Edinburgh), L.R.F.P.S. (Glasgow), 1938, Hawker, South Australia.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act, 1918*, of Tasmania, as duly qualified medical practitioners:

Alexander, William John Heriot, M.B., B.S., 1939 (Univ. Melbourne), Public Hospital, Launceston.

Dorney, Kiernan John Joseph, M.B., B.S., 1937 (Univ. Melbourne), Beaconsfield.

Colquhoun, Colin George Burrowes, M.B., B.S., 1923 (Univ. Melbourne), Longford.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Acts, 1925 to 1935*, of Queensland, as duly qualified medical practitioners:

Leval, Ludovic, M.D., 1930 (Padua), Brisbane.

Whyte, Alfred Moffatt, M.B., B.S., 1939 (Univ. Melbourne), Monto.

SOUTH AUSTRALIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act, 1919 to 1935*, of South Australia, as duly qualified medical practitioners:

Sheehan, Eleanor Marcella, M.B., B.S., 1924 (Univ. Melbourne), Education Department, Adelaide.

Blackwood, Kathleen Katrine, M.B., B.S., 1937 (Univ. Melbourne), Queen's Home, Adelaide.

Flaxman, Elizabeth Holden, M.B., B.S., 1937 (Univ. Melbourne), Children's Hospital, Adelaide.

Barker, John Edward, M.R.C.S. (England), L.R.C.P. (London), 1938, Northfield Infectious Diseases Hospital.

Honours.

BIRTHDAY HONOURS.

In the issue of May 17, 1939, we published a list of Birthday Honours conferred by His Majesty the King on Australian medical practitioners. From this list, by an unfortunate oversight, we omitted the name of Dr. G. A. C. Douglas, of Brisbane.

Dr. Douglas has been created an Officer of the Most Excellent Order of the British Empire. In congratulating Dr. Douglas on this honour we would also apologize for the omission of his name from our first list.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Sewell, Arthur Kenneth, M.B., B.S., 1939 (Univ. Sydney), 5, Deakin Avenue, Haberfield.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

Czerchowski, Tzrael, M.D., 1936 (Genoa), 17, Lang Street, North Carlton.

Books Received.

PHYSICIANS' FARE, by C. G. Learoyd; 1939. London: Edward Arnold and Company. Crown 8vo, pp. 302. Price: 7s 6d. net.

CANCER: CAUSATION, PREVENTION AND TREATMENT, by A. E. Blackburn, M.D.; 1939. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 116, with illustrations. Price: 6s. net.

LEAGUE OF NATIONS PUBLICATIONS. QUARTERLY BULLETIN OF THE HEALTH ORGANIZATION: VOLUME VII, Number 6, December, 1938. Geneva: League of Nations Publications Department; Australia: H. A. Goddard. Royal 8vo, pp. 162, with illustrations. Price: 2s. 6d. net.

Diary for the Month.

JULY 27.—South Australian Branch, B.M.A.: Branch.
JUNE 28.—Victorian Branch, B.M.A.: Council.
JUNE 29.—New South Wales Branch, B.M.A.: Branch.
JULY 4.—New South Wales Branch, B.M.A.: Council (quarterly).
JULY 5.—Victorian Branch, B.M.A.: Branch.
JULY 5.—Western Australian Branch, B.M.A.: Council.
JULY 6.—South Australian Branch, B.M.A.: Council.
JULY 7.—Queensland Branch, B.M.A.: Branch.
JULY 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JULY 14.—Queensland Branch, B.M.A.: Council.
JULY 15.—New South Wales Branch, B.M.A.: Ethics Committee.
JULY 19.—Western Australian Branch, B.M.A.: Branch.
JULY 20.—New South Wales Branch, B.M.A.: Clinical Meeting.
JULY 25.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 26.—Victorian Branch, B.M.A.: Council.
JULY 27.—New South Wales Branch, B.M.A.: Branch.
JULY 27.—South Australian Branch, B.M.A.: Branch.
JULY 28.—Queensland Branch, B.M.A.: Council.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes sought, etc., see "Advertiser", pages xvi-xix.

AUSTIN HOSPITAL FOR CANCER AND CHRONIC DISEASES, HEIDELBERG, VICTORIA: Resident Medical Officer.
CAIRNS HOSPITALS BOARD, CAIRNS, QUEENSLAND: Assistant Medical Officer.
CANTERBURY DISTRICT MEMORIAL HOSPITAL, CAMPSIE, NEW SOUTH WALES: Resident Medical Superintendent.
DEVON PUBLIC HOSPITAL, LATROBE, TASMANIA: Surgeon Superintendent.
INNISFAIR HOSPITALS BOARD, INNISFAIR, QUEENSLAND: Assistant Medical Officer.
KING GEORGE V AND QUEEN MARY MATERNAL AND INFANT WELFARE FOUNDATION: Investigation and Research Grants.
ROYAL SOUTH SYDNEY HOSPITAL, ZETLAND, NEW SOUTH WALES: Senior Honorary Physician.
SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Clinical Assistant.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phoenix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17.	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 173, North Terrace, Adelaide.	All Lodge appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	Wiluna Hospital. All Contract Practice Appointments in Western Australia.

Editorial Notices.

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